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List of abbreviations

AIDS	Acquired human immune-deficiency syndrome
ART	Anti-retroviral therapy
MDR-TB	Multidrug-resistant tuberculosis
M(X)DR-TB	Multi (extensively) drug-resistant tuberculosis
XDR-TB	Extensively drug-resistant tuberculosis

Chapter 1

1. Orientation to the study

1.1 Introduction

Tuberculosis is a chronic infectious disease caused by the bacillus Mycobacterium tuberculosis. Although the disease typically affects the lung, it can affect any part of the human body (Davies, Gordon & Davies 2014:130; Munsab, Santanu, Ravinder, Pradeep & Ankur 2013:123). According to the World Health Organisation (2014b:1), the bacillus Mycobacterium tuberculosis is transmitted through the air when a person with the disease coughs or sneezes. As a result, persons in the surroundings may become infected when they breathe in the bacteria. Given this mode of transmission, Dye (2015:4) describes tuberculosis as an airborne disease.

Davies, Gordon and Davies (2014:80) report that the Mycobacterium tuberculosis is a resistant bacterium that is protected by a lipid coat, and thus it can survive adverse conditions like acidic environments. Added to this, the bacteria have the ability to survive diverse environmental conditions. They are found widespread in the environment, particularly in soils and water (Davies et al 2014:48). The bacteria have the ability to survive for long periods in dust, especially in the dark, warm and moist environments as these environmental conditions protect them from the lethal effects of ultraviolet rays of the sunshine (Lucas & Gilles 2003:153). Moreover, the Mycobacterium tuberculosis has the ability to survive for years within the host in small but viable populations (Dye 2015:2).

Tuberculosis is an ancient disease (Fmusick 2004:6). Yet, the disease continues to be the leading cause of morbidity and mortality worldwide (Lewis & Sloan 2015:780; Zwerling, Hanrahan & Dowdy 2016: 407-409). Globally, tuberculosis is responsible for about 1.4 million deaths every year (Zwerling, Hanrahan & Dowdy 2016: 407-409). Moreover, the emergence of the MDR-TB makes the disease to be more challenging today (WHO 2016:1).

MDR-TB is a strain of tuberculosis that is resistant to the two most potent first line anti-tuberculosis drugs: rifampicin and isoniazid (Adams & Butterly 2015:1-2). This strain of tuberculosis affects both the clinical management of patients with the disease and patients' treatment outcomes (Caminero 2013:39-44). According to Pinto and Menzies (2011:129-30), about 17% of all new tuberculosis cases worldwide have some forms of drug resistance. Dheda and Migliori (2011:1) agree with this assertion and state that about 5-10% of global MDR-TB cases are extensively drug resistant tuberculosis. The extensively drug resistant tuberculosis (XDR-TB) is a form of MDR-TB that is resistant to the two most powerful anti-tuberculosis drugs, isoniazid and rifampicin, in addition to resistance to any of the fluoroquinolones (like levofloxacin or moxifloxacin), and one of the three injectable second-line drugs: amikacin, capreomycin or kanamycin (Dheda, Gumbo, Gandhi, Murray, Theron, Udwadia, Migliori & Warren 2014:321).

The empirical literature sources indicate that XDR-TB cases are present among patients with MDR-TB in Ethiopia (Agonafir, Lemma, Wolde-Meskel, Goshu, Santhanam, Girmachew, Demissie, Getahun, Gebeyehu & Soolingen 2010:1259-65). The prevalence of MDR-TB in newly notified tuberculosis cases has increased in Ethiopia from 1.6% in 2005 to 2.3% in 2014 despite the utilisation of the Directly Observed Treatment short course strategy (Federal Ministry of Health of Ethiopia (FMOH) 2014:2). Yet, there is a dearth of research in Ethiopia on the programmatic management of drug-resistant tuberculosis. Added to this, there is presently limited empirical evidence in Ethiopia, particularly in the Oromia Region, on the medico-socio-economic and demographic determinants of the process and outcomes of the treatment for MDR-TB. This gap in knowledge warrants the need to conduct this study that focuses on investigating treatment outcomes of patients with MDR-TB and its determinants at referral hospitals in the Oromia Region of Ethiopia.

1.2 Background

Tuberculosis is considered the second leading global cause of mortality in the context of infectious diseases (Nelson, Hesse & Croyle.2009:137). Acknowledging this, it is not surprising for tuberculosis to be consistently noted in the empirical literature sources to be responsible for illnesses among millions of people each year in the world (The Economist 2014:2; Yuen, Amanullah, Dharmadhikari, Nardell, Seddon, Vasilyeva, Zhao, Keshavjee & Becerra 2015:2334). Given this, tuberculosis can be safely described as a global public health problem that has been exacerbated by the emergence of MDR-TB and XDR-TB. Yet, the global response to this problem (tuberculosis and its variants) has been reported to be inadequate. In 2010, for example, from the globally estimated 650 000 cases of tuberculosis, less than 5% were tested for the MDR-TB (Toczek, Cox, du Cros, Cooke & Ford 2012:29). In 2012, only 9% of tuberculosis cases, considered at risk of MDR-TB, were diagnosed as MDR-TB, and only one in five of these cases were notified by the national tuberculosis programmes (Global Fund for Tuberculosis, HIV/AIDS and Malaria (GFATM): 2014:1).

Ethiopia is among the 30 countries in the world described by the World Health Organization (WHO) as high burden for both tuberculosis and MDR-TB (Biadglegne, Sack & Rodloff 2014:3; WHO 2014a: 147). This descriptor of 'high burden' is a function of the high prevalence and incidence of tuberculosis cases in Ethiopia. The 2010-2011 population-based national tuberculosis survey revealed that the prevalence of bacteriologically confirmed cases of tuberculosis were estimated at 277 per 100 000 population (Kebede, Alebachew, Tsegaye, Lemma, Abebe, Agonafir, Kebede, Demissie, Girmachew, Yaregal, Dana, Getahun, Fiseha, Meaza, Dirse, Timimi, Sismanidis, Tadolini & Onozaki 2014:635). The annual incidence of MDR-TB cases in Ethiopia for the year 2011 was estimated at 2,200 (WHO 2010: 24; Falzon, Jaramillo, Wares, Zignol, Floyed & Raviglione 2013:691). The incidence of all forms of tuberculosis in 2012 was estimated at 247 per 100 000 population (Federal Ministry of Health of Ethiopia 2013:12). While this is the case, the result of the tuberculosis drug-resistance survey of Ethiopia revealed an increase in the prevalence of MDR-TB among new tuberculosis cases from 1.6% in 2005 to 2.3% in 2014.

Added to this, the national prevalence of MDR-TB among previously treated tuberculosis cases was noted in the same survey to increase from 11.8% in 2005 to 17.8% in 2014 (Federal Ministry of Health of Ethiopia (FMOH) 2013:48; FMOH 2014:2).

The high prevalence of MDR-TB is a concern for the government of Ethiopia and healthcare workers, particularly those who are directly involved in the care and treatment of people with this disease. In fact, the government of Ethiopia considers tuberculosis as one of the top national diseases of public health importance. Despite this, the number of hospitals in Ethiopia with capacity to provide diagnosis and treatment services to people with this disease is not adequate (Falzon et al 2013:690). In 2014, only 6% (2,405) of all bacteriologically confirmed cases of tuberculosis had a drug sensitivity test (Biadglegne, Sack & Rodloff 2014:7). In the same year, 2014, only 39% (503) of the annual estimated prevalence of MDR-TB (1300) was notified by the national tuberculosis programme (WHO 2015:62). Given this, the government of Ethiopia expanded its treatment services for MDR-TB, including the diagnosis of this disease. It currently rolls out the programmatic management of drug-resistant tuberculosis across all the provinces of Ethiopia. Even though this is the case, only a few studies are available on the programmatic management of drug-resistant tuberculosis (Biadglegne, Sack & Rodloff 2014:3), and there are no studies to date on this programme in the Oromia Region of Ethiopia.

1.3 Motivation of the study

Researchers' interest and the need to solve practical problems are often the driving forces for researchers to engage in a study (Marczyk, DeMatteo & Festinger 2005:27-29). In this study, the researcher has an interest in developing an understanding of drug-resistant tuberculosis. This quest is a function of the high incidence and prevalence of drug-resistant tuberculosis in Ethiopia, which is therefore considered in the same as a public health problem.

As a clinical officer, the researcher provided clinical care to polyclinic attendants at two health centres in the Oromia Region of Ethiopia. As a result, the researcher frequently experienced first-hand health and economic problems faced by individuals affected by tuberculosis. Shortly, after graduating with a master's degree in public health in 2006, the researcher engaged in the programmatic management of tuberculosis and the human immune deficiency virus (HIV) in Ethiopia. Since then, the researcher worked on the tuberculosis and human immune deficiency virus (TB/HIV) programme at different healthcare levels in varied roles. These roles include site level technical support for health caregivers and clinical mentor support for caregivers working on the tuberculosis and HIV programme at health centres and hospitals. During his clinical practice, the researcher learned that some patients treated for tuberculosis failed to recover from this disease, particularly when treated using the generic first-line anti-tuberculosis drugs. This, in part, contributed to the emergence of the varied forms of tuberculosis such as MDR-TB in Ethiopia.

Thus, treatment centres for MDR-TB were set up in Ethiopia. During the researcher's regular visits to these centres in the Oromia Region, he noted that the management of MDR-TB was a challenging professional task. The researcher also learnt that there was no evidence on the determinants of the treatment outcomes of patients with MDR-TB. There was also no evidence regarding the patients' perceived quality of the care they were provided. These observations were the root of the researcher's inspiration for working on MDR-TB, and to conduct a study on this form of tuberculosis. Given this, the researcher

registered for a doctoral programme at the University of South Africa with the view to investigate treatment outcomes of patients with MDR-TB and its determinants, as it is a priority subject in the Oromia Region of Ethiopia.

1.4 Statement of the research problem

Tuberculosis has claimed more lives than any other infectious disease on earth during the past two centuries (Heemskerk, Caws, Marais & Farra 2015:1). The existence of tuberculosis is as old as human history (Hatfull & Jacobs 2014:31) but the development of MDR-TB as a public health problem is a recent phenomenon, which emerged in the early 1990s (Udwadia 2012:286). MDR-TB is the strain of tuberculosis bacilli that is resistant to the two most potent first-line anti-tuberculosis drugs, i.e. isoniazid and rifampicin (Caminero, Sotgiu, Zumla & Migliori 2010:621). Despite advances in treatment, prevention and control (vaccine, drugs and diagnostic measures), tuberculosis continues to be one of the major causes of morbidity and mortality worldwide (Lewis & Sloan 2015:779). This is particularly the case for MDR-TB. In 2013, a total of about 480 000 cases and about 210 000 deaths were caused by MDR-TB (WHO 2014a:70).

In 2016, the global disability-adjusted life-years for tuberculosis and MDR-TB was estimated. The disability-adjusted life-years for tuberculosis was calculated by summing up years of life lost to premature death caused by tuberculosis and years of productive life lost due to disability caused by tuberculosis. In this way the estimated disability-adjusted life-years for drug-susceptible tuberculosis was 39·9 million (uncertainty interval (UI):38·1 million to 41·9 million). For the same year, the estimated global disability-adjusted life-years for MDR-TB without extensive drug resistance was 3·32 million (UI=2·79 million to 3·91 million). The disability-adjusted life-years for extensively drug-resistant tuberculosis for the same year was 369 000 (UI=301 000–445 000) (Global Health Metrics 2017:1283).

Both tuberculosis and MDR-TB disproportionately affect people with conditions such as HIV, diabetes and malnutrition (Glaziou, Sismanidis, Floyd & Raviglione 2015:5; Rouzier,

Oxlade, Verduga, Gresely & Menzies 2010:1320). As such, MDR-TB is a serious threat to decades of global progress in the control of tuberculosis. This is because it negatively affects the diagnosis, clinical management and treatment outcomes of tuberculosis (Caminero 2013:39-44).

Ethiopia is one of the 30 high burden countries for tuberculosis, tuberculosis and HIV co-morbidity and MDR-TB. Ethiopia is one of the countries that are committed to develop and implement plans to achieve universal access to diagnosis and treatment for MDR-TB (Falzon, Jaramillo, Wares, Zignol, Floyed & Raviglione 2013:694). In Ethiopia, even though the incidence of MDR-TB among new cases increased from 1.6% in 2005 to 2.3% in 2014 (Federal Ministry of Health of Ethiopia 2014:2), the number of MDR-TB cases ever detected and enrolled on treatment has been far below the national incident estimate (WHO 2010: 24; Falzon et al 2013:690). Thus, the huge pool of individuals with untreated MDR-TB represents an important source of disease transmission (Kendall, Azman, Cobelens & Dowdy 2017:2). Thus, the government of Ethiopia is expanding the services on the programmatic management of MDR-TB to all its regions or provinces (Biadglegne, Sack & Rodloff 2014:3).

Treatment of MDR-TB has as high impact as prevention (Kendall, Azman, Cobelens & Dowdy 2017:10). However, there are certain factors that determine treatment outcomes of patients with MDR-TB. These factors challenge the desired impact of MDR-TB service expansion. The MDR-TB treatment causes extreme social, financial and employment hardship for the patient with the disease. Most patients with MDR-TB had to move home and leave their jobs, and face major stigmatisation (Baral, Aryal, Bhattrai, King & Newell 2014:1). Treatment of MDR-TB and XDR-TB can take up to two years (WHO 2011:1). The lengthy treatment duration is poorly tolerated and difficult to monitor (Van Deun, Maug, Salim, Das, Sarker, Daru & Rieder 2010: 684). Moreover, physiological disorders (such as adverse drug-reactions) that may result from the use of some second-line drugs can sometimes be fatal (Ministry of Health of Ethiopia 2014:122-5).

Poverty is an additional factor that affects the treatment process and the treatment outcomes of patients with MDR-TB. Poverty and food insecurity are both causes and consequences of tuberculosis (Rusen, Squire & Billo 2010:163; WHO 2013b:3). Poverty and under-nutrition can enhance an individual's vulnerability to tuberculosis and maintain the cycle of infection and disease (Uplekar, Weil, Lonnroth, Jaramillo, Lienhardt, Dias, Falzon, Floyd, Gargioni, Getahun, Gilpin, Glaziou, Grzemska, Mirzayev, Nakatani & Raviglione 2015:1799). Poverty related conditions like poor living conditions and under-nutrition may increase infection with tuberculosis and its progression to disease. For the poor, tuberculosis associated stigma, marginalisation, depression, and despair can amplify their poverty state and the disease, which is tuberculosis (Uplekar, Weil, Lonnroth, Jaramillo, Lienhardt, Dias, Falzon, Floyd, Gargioni, Getahun, Gilpin, Glaziou, Grzemska, Mirzayev, Nakatani & Raviglione 2015:1799). Therefore, without addressing the patient's social problems, the diagnosis and provision of free drugs may not directly lead to curing tuberculosis among the poor (Saunders & Evans 2015:1-2). Besides, the level of patient satisfaction with care can determine patients' adherence with treatment and the physician's advice (Punnakitikashem, Buavaraporn, Maluesri & Leelartapin 2012:1232). It is therefore not surprising to note that the measures of patient treatment outcomes frequently mentioned in the literature sources, include changes in patients' health status and the level of their satisfaction with care given (Longest 2015: 237-241). Yet, there is presently very limited empirical evidence in Ethiopia, particularly in the Oromia Region on:

- Factors determining treatment outcomes of patients with MDR-TB who are enrolled on second line anti-tuberculosis drugs.
- Patients' perceived quality of care and their satisfaction with care given for MDR-TB.

This gap in knowledge warrants the need to conduct this study. The study focuses on investigating treatment outcomes of patients with MDR-TB and its determinants at referral hospitals in the Oromia Region of Ethiopia. The generations of evidence in these areas will contribute towards designing appropriate interventional measures for averting factors associated with unfavourable MDR-TB treatment outcomes among patients with MDR-TB. Moreover, the evidence generated on factors that may determine patients' perceived quality of care and their satisfaction with care given for MDR-TB would help to institute

interventions that could enhance patient satisfaction and their adherence to treatment in the Oromia Region and the other regions of Ethiopia as a whole.

1.5 Aims, objectives and hypotheses of the study

Aims of the study

The aim of this study is two-fold. Firstly, the study aims to investigate the treatment outcomes of patients with MDR-TB and its determinants at referral hospitals in the Oromia Region of Ethiopia. Secondly, the study aims to develop a conceptual model for enhancing the treatment of patients with MDR-TB in the Oromia Region of Ethiopia.

1.5.1 Objectives of the study

1.5.1.1 Quantitative component objectives

1. Determine treatment outcomes of patients with MDR-TB who are enrolled on second line anti-tuberculosis drugs at the Adama and Nekemte Referral Hospitals.
2. Assess factors associated with observed levels of treatment outcomes among patients with MDR-TB.

1.5.1.2 Qualitative component objectives

1. Explore the perceived quality of care and satisfaction of patients with MDR-TB with the overall MDR-TB related care and services provided at the Adama and Nekemte Referral Hospitals.
2. Explore the perceptions and practices of caregivers for MDR-TB regarding the functionality of the programmatic management of drug-resistant tuberculosis at Adama and Nekemte Referral Hospitals.

1.5.1.3 Mixed method objectives

1. Explore how the data from the interviews with patients with MDR-TB help to explain any quantitative results observed at Adama and Nekemte referral hospitals
2. Explore how the data from the interviews with the caregivers for MDR-TB help to explain any quantitative results observed at Adama and Nekemte referral hospitals
3. Develop a conceptual model for enhancing the treatment of patients with MDR-TB in the Oromia Region of Ethiopia.

1.5.2 Hypotheses and research questions of the study

A research hypothesis outlines the plausible relationship between variables that the investigator expects to observe (Chasan-Taber 2014:32). In other words, a research hypothesis is a prediction of relationships between variables of a study. Examples of these variables include independent and dependent variables.

1.5.3 Quantitative component hypothesis

1.5.3.1 There is no relationship between the treatment outcomes of patients with MDR-TB and the demographic and socio-economic characteristics of patients with this disease, MDR-TB

1.5.3.2 There is no relationship between the baseline clinical characteristics of patients with MDR-TB and the treatment outcomes of patients with MDR-TB.

1.5.3.3 There is no relationship between adverse events from second-line drugs and the treatment outcome of patients with MDR-TB.

1.5.4 Qualitative component research questions

1.5.4.1 What could be the perception and satisfaction of patients with the overall MDR-TB related care and services provided at the Adama and Nekemte Referral Hospitals?

1.5.4.2 What could be the experience and practices of caregivers for MDR-TB regarding the functionality of the programmatic management of drug-resistant tuberculosis at Adama and Nekemte Referral Hospitals?

1.5.5 The mixed methods research questions

1.5.5.1 Do the data of the interviews with patients with MDR-TB help to explain any quantitative results observed at Adama and Nekemte referral hospitals?

1.5.5.2 Do the data of the interviews with the caregivers for MDR-TB help to explain any quantitative results observed at Adama and Nekemte referral hospitals?

1.6 Significance of the study

This study assesses multiple factors that may determine the process of MDR-TB treatment, adherence to treatment, patient satisfaction with treatment, and treatment outcomes of patients with MDR-TB. The knowledge that has been gained from this study may contribute to the enhancement of the treatment of patients with MDR-TB in the Oromia Region of Ethiopia. The outcomes of this study will serve as evidence to enable policy makers and health caregivers in the Oromia Region to make appropriate and timely decisions for supporting and treating patients with this condition. Such decisions may relate, for example, to the allocation of resources. This study develops a conceptual model that may be of practical utility for guiding healthcare workers in the provision of care and support services to patients with MDR-TB.

1.7 Conceptual and operational definitions

1.7.1. Definitions of key concepts

Drug-resistant tuberculosis

Drug-resistant tuberculosis is a strain of tuberculosis that is resistant to first-line anti-tuberculosis drugs (Caminero 2010:382). Strains that are resistant to only one first-line anti-tuberculosis drugs are referred to as mono-resistant tuberculosis (Caminero 2013:18). Strains that are resistant to more than one first-line anti-tuberculosis drug are designated as polydrug-resistant tuberculosis (WHO 2014b:18). The WHO assigned an additional form of drug-resistant tuberculosis called rifampicin resistant tuberculosis. Rifampicin resistant tuberculosis is a form of tuberculosis that is resistant to rifampicin in which the resistance to rifampicin is detected using phenotypic or genotypic methods, with or without resistance to other anti-tuberculosis drugs (WHO 2013a:5).

Multi drug-resistant tuberculosis (MDR-TB)

MDR-TB is defined as the Mycobacterium tuberculosis with in-vitro resistance to the two most potent first-line anti-tuberculosis medications, isoniazid and rifampicin (Hatfull et al 2014:413).

Extensively drug-resistant tuberculosis (XDR-TB)

This relates to the Mycobacterium tuberculosis with in-vitro resistance not only to isoniazid and rifampicin but also to other classes of medications commonly used to treat MDR-TB, i.e. the injectables and fluoroquinolones (Gunther 2014:280). There is also another form of drug-resistance level beyond MDR-TB. It is referred to as 'extremely' or 'totally drug-resistant tuberculosis' (XDR-TB) (Udwadia 2016:41-2; Behera 2012:190). Extremely or totally drug-resistant tuberculosis is defined as strains of the Mycobacterium tuberculosis that are resistant to all first and second-line anti-tuberculosis drugs (Tadolini, Centis, D' Ambrosio & Migliori 2012:105; Ribon 2015:31).

Health service quality

Health care quality is the degree to which health services increase the likelihood of desired health outcomes (Longest 2015: 237). Quality of health care is measured by certain attributes. These attributes include the knowledge and courtesy of caregivers (assurance), and their ability to deliver the promised care (assurance) (Pillai & Kumari 2016:80). The quality of health care is also measured by the caregivers' ability to care (reliability), and the quality of interaction between caregivers and patients (interpersonal quality) (Slonim & Pollack 2005:267). Another measure of health care quality includes caregivers' willingness to help patients (responsiveness) (Punnakitikashem, Buavaraporn, Maluesri & Leelartapin 2012:1232).

The physical facilities like the equipment and appearance of personnel (tangibility), the quality of patient service related to continuity of care, cost of service, accommodation and accessibility (structural quality), facility set ups including sanitation, overcrowding, availability of basic utility, place for recreation (physical quality) and courtesy, information, autonomy and caregiver's competence (process quality) are critical measures of quality of health care (Longest 2015:25). Added to this, Longest (2015: 237-244) considers patients' perception of quality and the status of patient satisfaction with care given as significant aspects of the measures of healthcare quality.

Patient's perceived quality of health care

Perceived quality is the patients' judgment about the overall excellence or superiority of healthcare services they receive. It is the measure of the discrepancy between the patient's expectations and their perception of the services given by an institution or by healthcare givers (Ramez 2012:131). Information from patients on the quality of healthcare is the best way to determine whether care aligns with their values, preferences, and needs (Tzelepis, Sanson-Fisher, CZucca & Fradgley 2015:831).

Patient satisfaction

Patient satisfaction is one of the patient reported measures of treatment outcomes (Mosadeghrad 2012:257). Patient satisfaction is determined by two factors. The first factor is patients' expectations. Patient expectations are services that the patients search and want to see in health institutions. The second factor is patients' perception of the services that they receive. Patient perceptions are measured on the basis of the opinions of patients about the services they receive and on the service production process (Dikmen & Yılmaz 2016:1048). The level of patient satisfaction with healthcare is one of the indicators used to measure quality of healthcare (Longest 2015: 241).

Patient adherence to treatment

Adherence is the extent to which a patient cooperates with his or her treatment regimen (Gebremariam, Bjune & Frich 2010:1). A patient is said to be adherent to treatment when he or she implements the medical instructions recommended by the healthcare giver. Patients who fail to adhere to their treatment are at an increased risk of morbidity and mortality. In addition, this category of patient is at risk of transmitting the disease to others (Ndwandwe, Mahomed, Lutge & Knight 2014:59). Certain factors are associated with patients' non-adherence to treatment. These include lack of education, unemployment and low socio-economic status. Personal factors like drug and alcohol use, presence of HIV and perceived severity of illness are risk factors for non-adherence to treatment (Sang, Obwoge, Kangethe, Ayiro & Changeiywo 2017:329).

Patient treatment enablers

Treatment enablers for patients with MDR-TB include the provision of incentives such as covering cost of transportation, provision of accommodation and food packages. These incentives or enablers can increase patients' adherence to treatment (Lange, Abubakar, Alffenaar, Bothamley, Caminero, Carvalho, Chang, Codecasa, Correia, Crudu, Davies, Dedicoat, Drobniewski, Duarte, Ehlers, Erkens, Goletti, Gùnther, Ibraim, Kampmann, Kuksa, Lange, Leth, Lunzen, Matteelli, Menzies, Monedero, Richter, Rùsch-Gerdes,

Sandgren, Scardigli, Skrahina, Tortoli, Volchenkov, Wagner, Werf, Williams, Yew, Zellweger & Cirillo 2014:45).

1.7.2. Operational definitions

Operationalization is the process of moving from a construct's conceptual definition to specific activities or measures that allow a researcher to observe it empirically. An operational definition of a variable changes it into a specific operation or action so that it can be measured in the empirical world (Neuman 2014:207). Operationalization eliminates confusion in meaning and communication. It ensures researchers to precisely define what is to be measured or observed and how the measurement or observation will be carried out (Lancaster 2005:23).

Patient registration group

Patients with MDR-TB are registered for treatment based on their previous treatment history. Patients are registered under two broad categories of registration groups: new registration group and previously treated registration group. A patient is said be in a new registration group if he or she has never received anti-tuberculosis treatment or has received anti-tuberculosis treatment for less than 1 month. Patients in the previously treated registration group include those who have relapsed (relapse patient with tuberculosis), patients treated after lost to follow ups. The relapse patient with tuberculosis group relates to patients who have successfully completed treatment for tuberculosis at some point in time but were later diagnosed with the disease (Federal Ministry of Health) (FMOH 2014:45). With regard to the lost to follow ups group, this relates to patients with tuberculosis who after taking treatment for the disease for more than one month became lost to follow ups for two months or more months, but later re-commenced treatment for active tuberculosis. Treatment after failure is that group of patients who remain sputum or culture positive at five or more months after commencing anti-tuberculosis treatment. There are also some groups of patients with tuberculosis registered under the 'other previously treated' group of patients. These are patients who have previously been treated

for tuberculosis but whose most recent treatment outcome for tuberculosis is not known or is not documented.

Adverse drug reactions

Adverse drug-reactions are unwanted responses to a medicine. Common adverse drug-reactions from the use of second-line anti-tuberculosis drugs include myelosuppression, anemia, neutropenia, peripheral and optical neuropathy (Caminero et al 2010:627). Moreover, hypothyroidism, Hypokalemia, electrolyte wasting and renal insufficiency are common adverse drug-reactions among patients treated for MDR-TB. These reactions are usually noxious and unintended (Caminero 2013:141). The adverse drug reactions can lead to non-adherence to treatment. Thus, the occurrence of adverse drug-reactions can contribute to morbidity, and treatment failure (WHO 2014b:167).

Baseline clinical and laboratory tests

Baseline clinical and laboratory tests are done for each patient with MDR-TB. The tests are used both for signs of the efficacy of the treatment given for MDR-TB and also to monitor the adverse drug reactions (Federal Ministry of Health of Ethiopia 2014:74). Baseline clinical and laboratory tests for patients with MDR-TB are the requirements for patients with MDR-TB before the initiation of second-line anti-tuberculosis drugs. Baseline clinical tests done for patients with MDR-TB include physical examinations, taking vital signs, the determination of baseline malnutrition and identification of co-morbidities with MDR-TB. Moreover, the baseline laboratory tests done include the sputum smear examination, sputum culture and the drug-sensitivity test. Baseline laboratory tests also include serum potassium level, creatinine, and renal as well as liver function tests. They also involve the HIV test, pregnancy and the thyroid-stimulating hormone tests. Furthermore, patients co-infected with HIV are eligible for the complete blood count and the T-lymphocyte cell bearing (CD4) count. Most of the clinical and laboratory tests are carried out at baseline and monthly thereafter. This study assessed the status of patient monitoring against the nationally set standard to monitor patients clinically and through laboratory tests (Federal Ministry of Health of Ethiopia 2014:76).

Patient's baseline risk factor

This focuses on the patients' baseline record on certain risk factors that are believed to affect patients' adherence to treatment and ultimate treatment outcomes (Djibuti, Mirvelashvili, Makharashvili & Magee 2014:1; HerreroI, RamosI & ArrossiI 2015:295). These factors include age, sex, household location, size of family, patient employment status, alcohol use, presence of co-morbid conditions, and history of imprisonment. In addition, the patient's HIV status and previous treatment history for tuberculosis or MDR-TB are considered to be risk factors.

MDR-TB treatment outcomes

These relate to the outcomes of treatments given for MDR-TB. Examples of these include interim treatment outcomes, cured, treatment completed, treatment failure, lost to follow ups and died. The interim treatment outcome of patients with MDR-TB is evaluated at six-months after the initiation of treatment. The treatment outcome at month six is evaluated as one of the following. These include culture converted, died, lost to follow ups and not evaluated.

Cured is one of the standard treatment outcomes for patients with MDR-TB. A patient is classified as cured if he or she has completed treatment according to the national recommendation standard without evidence of failure and three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase of treatment.

A treatment completed patient with MDR-TB is that patient who completed treatment according to the national recommendation without evidence of failure but no laboratory record indicated that three or more consecutive cultures taken at least 30 days apart were negative after the intensive phase of treatment.

Treatment failure

According to the WHO (2014b:20), treatment of patients with MDR-TB is said to have failed if treatment is terminated or when the patient needs a permanent regimen change for at least two of the anti-tuberculosis drugs because of:

- lack of conversion by the end of the intensive phase; or

- bacteriological reversion in the continuation phase after conversion to negative; or
- evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs; or
- adverse drug reactions.

Died

A patient who dies for any reason during the course of treatment for tuberculosis is given the treatment outcome of 'died' (WHO 2013a:6).

1.8 The theoretical framework of the study

A theory consists of a series of tentative premises about ideas and concepts that lay the foundation for any empirical research endeavour on a given phenomenon (Imenda 2014:185). A theory is formulated based on existing observations and insights. On top of serving as an overarching foundation for explaining research processes, a theory provides an inspirational framework that guides the research (Crano, Brewer & Lac 2015:5-6). A conceptual framework on the other hand, is a set of interrelated concepts that shows the way in which a phenomenon of interest is viewed (Imenda 2014:186). It serves as an orientation lens through which a research endeavour is seen (Holloway & Wheeler 2010:11). Conceptual frameworks are often derived from a theoretical framework(s), and sometimes developed by the researcher. According to Marczyk, DeMatteo and Festinger (2007:31), a conceptual framework is a description of a phenomenon of interest that attempts to show the relationships between constructs we know about the phenomenon. Conceptual frameworks consist of tentative premises about concepts in a research study. Researchers select testable research hypotheses from these premises regarding relationships among variables, and it is these hypotheses that are often subjected to research scrutiny (Crano et al 2015:5-7).

This study employed a mixed method design in which both quantitative and qualitative data are used to address its aims and objectives. Given this, this study required an overarching framework to guide its research process. Thus, following a careful

examination of the different theoretical frameworks available, this study opted for the Donabedian framework to measure health service quality (see figure 1.1). The rationale behind using the Donabedian framework was that the framework was congruent to the aims and objectives of this study. This framework enabled the researcher to measure the different dimensions of health service quality assessed in this study.

The Donabedian framework for measuring the performance of a healthcare, addresses factors that determine the performance of healthcare in three fundamental parts (structure, process and outcome) (Berwick & Fox 2016: 239). In the Donabedian framework, healthcare structure means the physical and organizational characteristics of health facilities where health care is provided. The process includes the services and treatments that the patient receives. The outcome is the result achieved by the treatment of the patient (Višnjić, Veličković & Jović 2012:54).

In this study, socio-demographic and socio-economic characteristics of patients constitute the structure part of the Donabedian framework. Likewise, the status of the availability and functionality of the patient support schemes and conditions of the service set-ups and conditions of the staffing constitute the structural part of the framework. Similarly, the process includes all factors that focus on the patient treated for MDR-TB. These include the patient-centredness of care and the conditions of interpersonal communication between patients and their caregivers, the level of responsiveness of the care given to the patients and the respect given for patients with MDR-TB. The process also incorporates patient adherence to treatment. Factors that directly influence the process of the care that patients receive, including patients' clinical characteristics (age, sex, body mass index, comorbidities) and the occurrence of adverse events from second-line drugs, are considered to be part of the process part of the framework used in this study. Moreover, the treatment outcomes of patients with MDR-TB, patients' level of perceived quality of care and patient satisfaction with care given for MDR-TB constitute the outcome part of the framework.

The Donabedian framework is noted in the literature to contribute to the safety of patients by opening new approaches in healthcare that ensure patients' safety and meet patients' health needs. The framework helps healthcare workers to understand the potential risks of healthcare to the health of patients (Višnjić, Veličković & Jović 2012:54-55). In this study, the framework enabled the researcher to measure the various factors that determined the functionality and quality of the healthcare service provided to patients with MDR-TB. This in turn helped to answer the specific questions of the study, i.e., factors determining the treatment outcomes and the satisfaction of patients with MDR-TB with the healthcare they received.

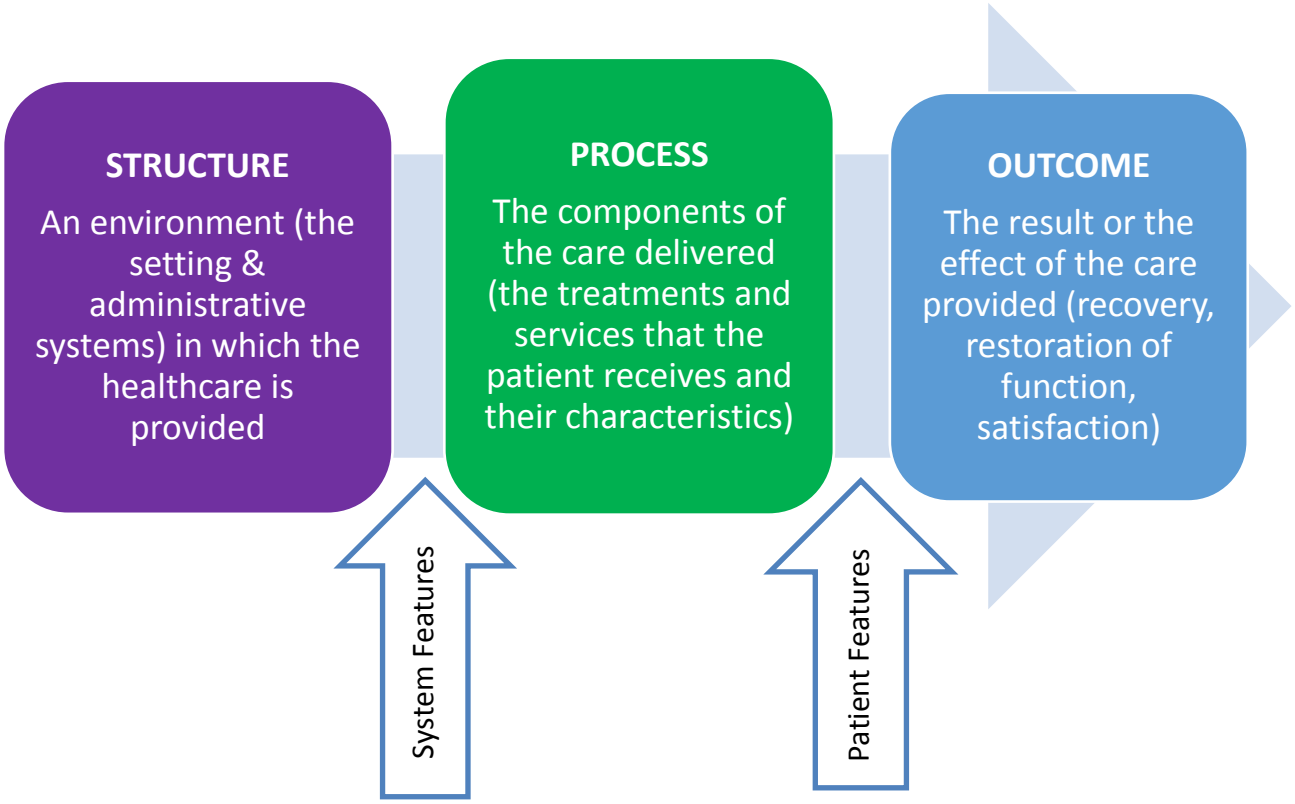


Figure 1. 1 The Donabedian Framework (Source: Višnjić, Veličković & Jović 2012:54-55)

1.9 The Donabedian framework for healthcare quality

Quality of healthcare is the degree to which health services that are required to serve individuals and populations increase the likelihood of desired health outcomes that are consistent with the contemporary professional knowledge (Donabedian 1988:1743). In this context, quality of healthcare is defined in terms of the technical and interpersonal quality of healthcare. Technical quality stresses that the desired health outcomes sufficiently exceed anticipated health risks. Interpersonal quality is concerned with whether patients are treated in a humane and culturally appropriate or congruent manner. The interpersonal component of quality requires that the followings be maintained (Longest 2015: 240-41):

- ✓ Patients' values and preferences.
- ✓ Patients' physical comfort, including pain control.
- ✓ Patients' emotional and psychological comfort, including alleviation of fear and anxiety.
- ✓ Patients' need for information and open communication with caregivers.

1.9.1. Components of the healthcare quality

Quality of healthcare can be divided into three distinct but interrelated components (Ayanian & Markel 2016:206). These are the structure, the process and outcome measures of quality. Structural quality includes factors that affect the conditions in which the healthcare occurs. Process quality is related to how the caregiver behaves towards patients, whether the patient is treated with respect and is involved in the treatment decision-making. The outcome measures of quality focus on changes in the patient's health status, behaviour and satisfaction. These three dimensions of healthcare quality affect patients' perception of quality and their satisfaction with the quality of care they are provided (Kajonius & Kazemi 2015:1-2).

1.9.2. Structural Quality

The structure encompasses the setting, the qualification of the caregivers and the policy and administrative system in which the healthcare is provided (Ayanian & Markel 2016:206).

In the context of the programmatic management of drug-resistant tuberculosis, the structure refers to the tangible attributes of the hospital premises where patients are cared for. It includes the hospital environment and the personnel involved in the care of patients with MDR-TB. The cleanness of the environments (buildings) of the hospital and treatment centres for MDR-TB and the facilities and amenities which can influence the patients' satisfaction with care given. Similarly, the quantity and quality of the healthcare personnel that create the capacity to provide optimum healthcare services can influence patients' perceived quality of care and patient satisfaction with care given for MDR-TB (Mosadeghrad 2012:253). The health system should be organized in a way that does not only guarantee the provision of optimum care on a continuous basis, but it should also be organized to the needs, values and expectation of patients (WHO 2014:132). Moreover, for a well-organized health system to provide the care needed, there should exist ready and motivated caregivers (Arakawa, Arcêncio, Scatolin, Scatena, Ruffino-Netto & Villa 2011:1000). Physical facilities of the service setups, equipment used and the appearance of personnel providing the intended service can influence the perception of patients with regards to the quality of service received, including their satisfaction with the service (Ramez 2012:132).

1.9.3. Process quality

One approach to the assessment of healthcare quality is to examine the process of care rather than its outcomes (Ayanian & Markel 2016:206). This is justified by the assumption that one is interested not in the power of medical technology to achieve results, but in whether what is known to be "good medical care" has been applied. Process quality focuses on the way healthcare is coordinated, the continuity of the care provided, and whether the care is acceptable to the recipients (Višnjić, Veličković & Jović 2012:55). Compared to outcome measures of quality, the measurement of process quality is more

relevant to measure whether healthcare practice is appropriately applied (Donabedian 2005:694-5).

In the MDR-TB treatment setting, factors that may determine the quality of the process of the care that is provided to patients with MDR-TB include caregivers' empathy, efficiency and effectiveness of the care. Empathy refers to the ability of the healthcare setting in understanding the needs of patients with MDR-TB and providing the care they need. Efficiency is the optimum use of available resources in the way that maximizes the benefits of patients with MDR-TB. Effectiveness focuses on the short-term clinical and non-clinical outcomes of patients treated for MDR-TB. This includes patients' perception of the care they receive and their cooperation in treatment decision-making. As such, process quality deals with whether the diagnosis, care, and treatment given to patients with MDR-TB achieve the desired outcomes from the patients' perspectives (Višnjić, Veličković & Jović 2012:55). The level of healthcare effectiveness is an important attribute in determining satisfaction with the care of patients with MDR-TB (Mosadeghrad 2012:257).

1.9.4. Outcome quality

Outcome quality focuses on the efficacy of the clinical and non-clinical interventions on the quality of life and well-being of patients with MDR-TB. Patient satisfaction with healthcare could not be a good indicator of quality in relation to the technical clinical care because patient satisfaction is influenced more by the process elements of healthcare like the way in which the patients' needs are preferences are accommodated and the comfort of the physical surroundings than the technical quality that relates to the effectiveness of the care given in producing the achievable health gain. The final and long-term outcomes of the diagnosis, care, and treatment given to the patient are expected to achieve the desired standard clinical outcomes of patients with MDR-TB (Mosadeghrad 2012:257). As such, the outcomes of healthcare are changes in the health status of individuals, which are attributable to interventions (Eldar 1999:75). The extent to which the agreed-upon desired results are achieved is the ultimate test of the assumptions inherent in the use of the structure and process in the assessment of the quality of healthcare. Outcome measures

of the healthcare quality describe the result achieved by the treatment of the patient. The outcome measures of medical care include recovery, restoration of function or healing, patient survival and mortality (Višnjić, Veličković & Jović 2012:54-5). The majority of the outcome measures of the results of medical care are fairly concrete. As such, outcome measures of medical care (e.g. death) are apparently amenable to more precise measurement (Donabeidn 2005: 692-3). Yet some of the outcome measures of healthcare are not clearly defined and are difficult to measure. These include patient attitudes, satisfaction, social restoration and physical disability and restoration (Donabedian 2005:693).

In summary, quality indicators are grouped into three categories. These include external indicators like the voice of patients or service users, process indicators like the voice of employees in the health system, and balanced indicators like programme monitoring from different angles. At different levels there is interdependence and causal relationships among the quality indicators. In that case, the holistic approach to measuring quality is appropriate. This is because a good structure can increase the likelihood of a good process. In turn, a good process has the potential to increase the likelihood of a good treatment outcome (Donabedian 1988:1745). In this way, a single indicator may not indicate the status of the entire quality of the healthcare. An outcome of healthcare may, however, have an influence on the process. While outcome is a good indicator of the result of healthcare, it does not indicate some aspects of outcome like the level of satisfaction of patients and their caregivers. Thus, it is important to focus on all of its essential elements while measuring quality of healthcare (Ayanian, & Markel 2016:206).

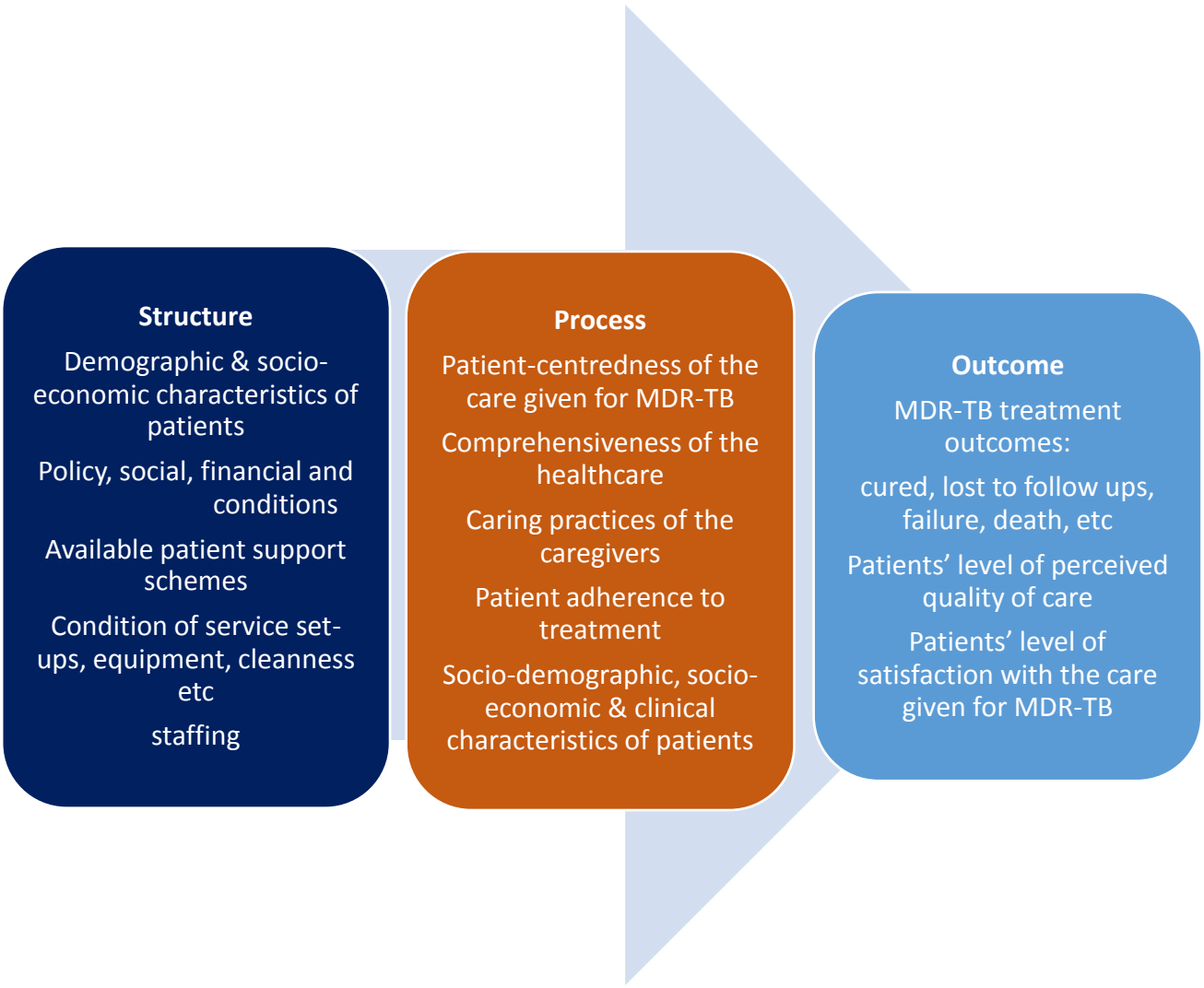


Figure 1. 2 : Conceptual framework of factors determining treatment outcomes of patients with MDR-TB and patient satisfaction (Source: Višnjić, Veličković & Jović 2012:54-55)

1.10 The research paradigm - its assumptions

Researchers are required to commence research with assumptions that are aligned with the research methodology, methods of data collection and analysis (Creswell, 2014:3-4). The researchers' assumptions that guide the conduct of a research study, are sometimes referred to as paradigms (Morgan 2007:49; Wagner, Kawulich & Garner, 2012). A paradigm is a set of beliefs that guide researchers through the research process (Morgan, 2014:1045-7). It is a system of presuppositions within a research approach and it forms the framework within which solutions are sought for a research problem (Almekinders, Beukema &Tromp 2009:253).

A paradigm is informed by philosophical assumptions about the nature of the truth or reality about a phenomenon (ontology), the researchers' position or stance in understanding the truth or reality of that phenomenon (epistemology), the values that researchers may attach or react to, the entire research process and the phenomenon under study (axiology) (Creswell, 2014:26). There are commonly agreed worldviews. These are positivism, post-positivism, constructivism, transformative and pragmatism worldviews (Saunders, Lewis & Thornhill 2007:102). These world views are the 'legitimated ways of knowing' (Bridges 2017:350). The ontology, axiology and epistemology that a research endeavour adopts, are framed in terms of the choice made among the available research philosophies. As such an overarching goal of any research endeavour is to achieve valid outcomes using appropriate scientific methods (Edmonds & Kennedy 2017:4). This study utilises a mixed methods design, specifically, it uses a concurrent mixed methods design. This design, like other mixed methods designs, combines quantitative and qualitative methods of inquiry. This indicates that the logic of inquiry in mixed methods designs includes both induction and deduction (Edmonds & Kennedy 2017:178). Thus, for a researcher pursuing knowledge development using a concurrent mixed methods design, the pragmatic paradigm is the paradigm of choice for a number of reasons.

Pragmatism offers an alternative worldview to positivism or post-positivism and constructionism. Pragmatism focuses on problems to be researched and the

consequences of the research (Feilzer 2010:7). Quantitative methods collect quantitative or objective data. But quantitative methods do not recognize the individuality of the participants or their experience (Gunasekare 2015:364).

In this study, an insight into the lived experiences of patients with MDR-TB on the care and services given to patients with this condition have positive benefits for the patients. These benefits need to be considered not only from the medical point of view but also from the individual patient's points of view. For any medical intervention to be of benefit to people, it should not only focus on its effectiveness to treat a disease, but also focus on its acceptability to the people affected by the diseases (Ellis 2010:108). The pragmatic paradigm allows researchers to use a mixture of methods to address a research problem. So, this study explored the individualistic views of patients' while collecting objective data in relation to MDR-TB.

This study focuses on treatment outcomes of patients with MDR-TB and its determinants. It explored patients' perceived quality of care and their satisfaction with care given for MDR-TB. The study also collected objective data with the help of quantitative methods in relation to MDR-TB. The rationale for this was to develop deeper understanding of treatment outcomes of patients with MDR-TB and its determinants. Such an understanding can be achieved if qualitative and quantitative methods are combined or mixed. A pragmatic paradigm allows the mixing of methods, as it recognizes the connection between theoretical and practical discourse (Conant & Zeglen 2002:3). Achieving a deeper understanding of treatment outcomes of patients with MDR-TB and its determinants, the researcher stresses, will facilitate an evidence-informed decision in the management of patients with MDR-TB in the Oromia Region of Ethiopia.

The pragmatic paradigm employed is compatible or congruent with the study's methodology, methods of data collection and analysis. It enabled the researcher to link the research questions, theories used, and the participants' experiences and practices (Misak 2013:21). In the context of health programmes, the current demands to demonstrate

evidence-informed programming and programme effectiveness fosters a competitive programmatic environment (Pearson, Field & Jordan 2007:8). In this regard, mixed-methods studies are capable of providing defensible evidence and an understanding of the programme context. Moreover, mixed methods research enables researchers to track the process and outcome of health programmes. A philosophical underpinning that facilitates such activities of tracking processes and outcomes of health programmes is a pragmatic paradigm. It is therefore employed in this study to inform the research design, including the research questions and objectives, and methods of data collection and analysis. This section will be discussed in chapter 3 in more detail.

1.11 Research methodology and the research design

1.11.1. Research Methodology

The healthcare setting is a dynamic social context in which people, organizational and clinical factors interact to affect health. Therefore, healthcare research often uses a pragmatic approach to conceptualise evidence (Fertman & Allensworth 2010:10). The researcher believes that the role of any research attempt should be on the utility of research outputs to solve real world problems (Mertens 2015:79; Feilzer 2010:8-9). As such, this study used a mixed methods methodology in which quantitative and qualitative approaches are combined. This methodology uses both deductive and inductive approaches to test the different hypotheses of the different segments of the same research problem. The deductive (quantitative) approach is meant to test the plausible relationship between the independent and dependent variables regarding the empirical observations of the study. The inductive (subjective and contextual) approach is used to understand the subjective meanings attached to the reality under investigation.

This study uses a pragmatic methodological approach with the assumption that the approach enables the best use of the study results to address the problem under investigation. This study aims to understand the complexity of the research problem under investigation through measuring both its objective and subjective layers. As such, this study uses a mixed methodology whereby both quantitative and qualitative approaches

are used to describe both the objective and subjective components of the same research question.

The rationale behind the choice of both quantitative and qualitative approaches for this study is based on the assumption that the phenomena under investigation has both objective and subjective layers. Thus, knowledge of both the observable (objective) and the subjective meanings of the phenomena under investigation are needed to fully understand the problem under investigation (Saunders, Lewis & Thornhill 2009:119). For the phenomena investigated in this study, the use of both objective and subjective inquiry produce knowledge that best represent the phenomena under investigation (Gunasekare 2015:362-3; Ihuah & Eaton 2013:937). The two methods complement each other (Edmonds & Kennedy 2017:231). This methodology seeks elaboration, enhancement, illustration and clarification of the results from one method with the results from the other method (Wei & Lin 2017:99). Thus, the quantitative and qualitative research results neither confirm nor refute each other but rather they are used to complement each other. Complementary helps to avoid limitation of the knowledge gained from one type of data that a quantitative or qualitative method alone can produce (Patton 2006:33). Complementarity is the ability of one type of method to compensate for the weaknesses of the other. The mixed methods methodology employed here combines the strengths of the two methods: quantitative and qualitative (Greene 2006:96). The specific research design used in this study is a concurrent mixed methods design.

1.12 The concurrent mixed methods research design

A research design is a thoughtfully constructed link between the purposes of a research study and the strategies used to implement it (Creamer 2018:59). Generally, a research design is a plan detailing how research will be conducted, and it guides the researcher in planning for and implementing a study (Groat & Wang 2013:24).

Creswell (2012:540) identifies six types of commonly used mixed methods designs. These include the:

- parallel (concurrent) design
- explanatory sequential design
- exploratory sequential design
- embedded or nested design
- transformative design
- multiphase design

From these available options, this study adopted a concurrent mixed methods design.

The concurrent design is characterized by its use of one data collection phase. That is both quantitative and qualitative data are collected simultaneously (Creswell 2012:540-1). Within the attempt made to answer the same research question, the purpose of using a concurrent qualitative method is to address a question that cannot be addressed by the dominant method, qualitative or quantitative (Gunasekare 2015:364). The qualitative quantitative methods often address different questions within the same phenomena under investigation. The mixing of the data generated from the two methods integrates the information gained from one method with that obtained from the other method. This integration of information is typically accomplished in the discussion and recommendation section of this study (Creswell 2009:2014:15).

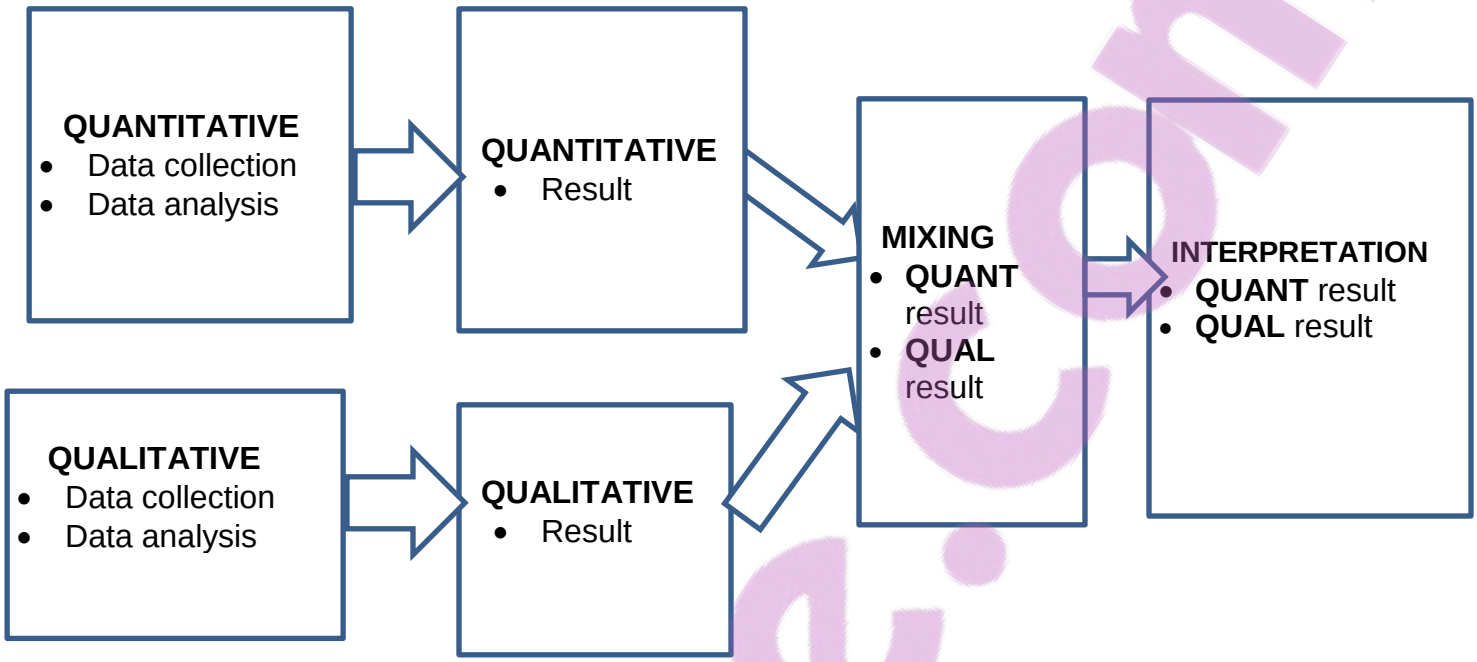


Figure 1. 3: Graphic representation of the concurrent mixed methods design used in this study (Source: Edmonds & Kennedy 2017:183).

1.12.1. Rationale for using a concurrent mixed methods design in this study

In relation to the concurrent mixed methods design employed in this study, there are two components: qualitative and quantitative. The concurrent mixed methods design served a complementarity function, that is, it was used to elaborate more on the quantitative study results. The study was conducted in one phase. That means that the quantitative and qualitative data were collected during a similar time period.

The rationale behind collecting both quantitative and qualitative data in this study was that the sub-research question under investigation had both quantitative and qualitative layers. Therefore, some of the study questions needed quantitative (objectives) data while the other study questions needed qualitative (subjective) answers. Thus, the two methods were used to study the different aspects of the same research problem (Ponce & Pagán-Maldonado 2015:119).

The quantitative component was used to assess the treatment outcomes of patients with MDR-TB and its determinants for patients with MDR-TB enrolled for treatment with second-line anti-tuberculosis drugs. Quantitative data cannot provide detailed information about the context in which individuals provide information for example, the setting. Therefore, in this study the qualitative component was used to explore the perceptions of patients with MDR-TB on the care they receive for MDR-TB and their satisfaction. The qualitative component also explored the perceptions and practices of caregivers for MDR-TB regarding the programmatic management of MDR-TB at Adama and Nekemte referral hospitals.

Quantitative and qualitative data were collected and analysed separately. Then the two data sets were integrated at the result stage and stage of discussion and interpretation of the study results. Then the discussion and recommendation were made regarding factors determining the treatment outcomes of patients with MDR-TB, patients' perceived quality of care and patients' satisfaction with care given for MDR-TB. The discussion was based on both quantitative and qualitative results (Teddlie & Tashakkori 2006:14).

By avoiding the biases intrinsic to using one method alone, the two strategies helped to complement each other (Flick 2009: 27). The one type of data supplies strengths to offset the weakness of the other form. In this way a more complete understanding of the research problem resulted from collecting both quantitative and qualitative data (Creswell 2012:540-1). From this, it is believed that a stronger recommendation and development of a conceptual framework for enhancing the management of patients with MDR-TB at referral hospitals in the Oromia Region of Ethiopia is made (Creswell 2012:540).

1.13 Sampling and sampling methods

A sample is a set of cases drawn from a larger study population with the aim of estimating the characteristics of the larger set or population (Andy 2009:49). This study used a mixed methods research design. As such, the sampling used for the study had two components. These were quantitative component and qualitative components.

1.13.1. Sampling: quantitative component

The source population for this study was all patients with MDR-TB enrolled for treatment with second-line anti-tuberculosis drugs at all treatment initiating centres in the Oromia Region of Ethiopia. As it was not practical to access all patients on treatment for MDR-TB in the Oromia Region of Ethiopia, patients enrolled for MDR-TB treatment and their caregivers at the two referral hospitals formed the accessible population of the study. As a result, the study population of this study was all patients with laboratory confirmed MDR-TB enrolled for MDR-TB treatment with second-line anti-tuberculosis drugs at the two referral hospitals in the Oromia Region of Ethiopia (Sumerson 2014:64). All members of this patient group fulfilled the inclusion criteria of the study and were potentially eligible for inclusion in this study. It was assumed that every member of the study population had the special characteristics of the samples (see inclusion criteria) needed to examine the factors under investigation. Hence, the entire study population was included in the study and thus surveyed (Holloway et al

2010:137-38). The patients included in the study are representative of the population of patients with MDR-TB (Hulley, Cummings, Browner, Grady & Newman 2013:25). Procedures followed in the selection of the sample for the quantitative component of the study are depicted in figure 1.4.

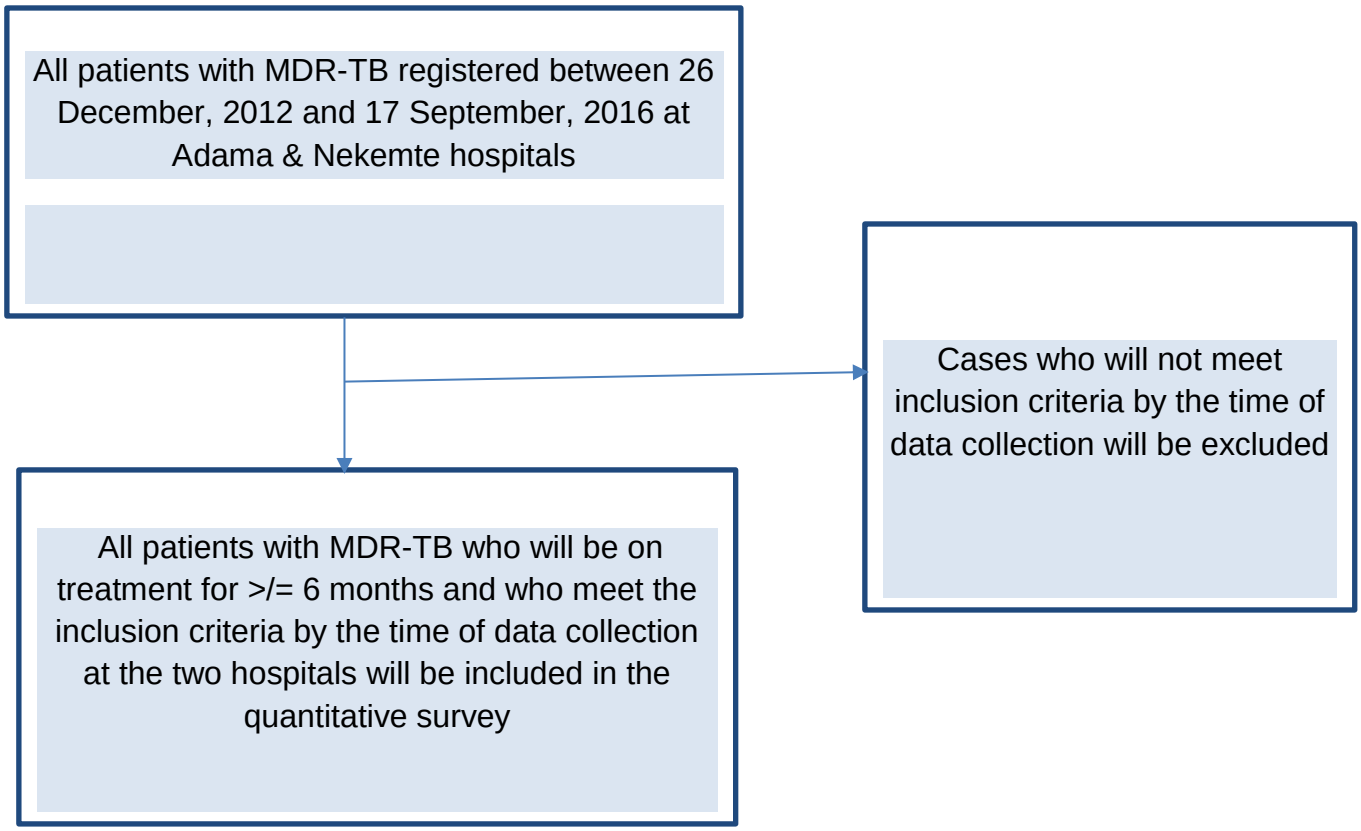


Figure 1. 4: Diagrammatic representation of the selection of patients with MDR-TB for the quantitative survey

1.13.2. Sampling: qualitative component

Perceptions of patients with MDR-TB on the quality of care given for MDR-TB and their satisfaction with the care was explored through a qualitative inquiry from patients aged 18 years and above. To enhance understanding of the perceptions and satisfaction of patients, participants that are presumably rich in the information needed were selected purposefully.

Purposive sampling is based on the idea that the sample is selected in relation to some criteria (inclusion criteria) which are considered to be important for that particular study.

Purposive sampling is also chosen for the reasons of convenience and low costs (Singh 2006:91; Kothari 2004:17). In this study, the use of the purposeful sampling method enables the researcher to select all participants that meet the criteria for inclusion in the study (Etikan, Musa & Alkassim 2016:2). As such, this study included information rich patients with MDR-TB in the semi-structured in-depth interviews with patients with MDR-TB. Moreover, caregivers for MDR-TB at the two study hospitals were selected purposively and included in the in-depth interviews based on their unique knowledge on the management of MDR-TB.

1.14 Methods of data collection

1.14.1. Quantitative data collection

The quantitative data were collected from the medical records (patient clinical charts, the unit MDR-TB register and patient treatment cards) using a structured questionnaire. Socio-demographic and clinical data were collected from patients with MDR-TB who were enrolled for treatment with second-line anti-tuberculosis drugs. Quantitative data were collected on patient socio-demographics, co-morbidities at baseline, baseline sputum smear and culture status, patient diagnostic modalities, patients' drug sensitivity test patterns and their history of treatment for tuberculosis. Quantitative data were also collected on patients' HIV sero-status and thereby the T-lymphocyte cell bearing (CD4) count and the status of the use of cotrimoxazole preventive therapy and the anti-retroviral therapy for MDR-TB and HIV co-infected persons. Data on adverse drug-reactions from second-line drugs and patient's interim and final treatment results, including the hospitals' practice of MDR-TB infection control were also collected.

1.14.2. Qualitative data collection

Qualitative data were collected from patients with MDR-TB and their caregivers. A semi-structured interview guide was used to collect data. The semi-structured interview guide included a number of areas:

- The perceptions of patients with MDR-TB on the health and economic impact of MDR-TB.

- The status of the availability of patient support schemes, patients' perceptions on availability of care that meets patients' expectations, patients' perceived quality of care and their satisfaction with care given for MDR-TB.
- The perceptions and practices of caregivers for MDR-TB and their experiences regarding the programmatic management of drug-resistant tuberculosis.

1.15 Methods of data analysis

1.15.1. Quantitative data analysis

The quantitative data were analysed using SPSS. The plausible relationships between the independent variables like patients' socio-demographic and clinical characteristics and the treatment outcomes of patients with MDR-TB were quantitatively analysed (Andrew & Halcomb 2009:121). A detailed discussion of the analysis is presented in chapter three.

1.15.2. Qualitative data analysis

The reported perceptions and experience of patients with MDR-TB and the experience and practice of caregivers for MDR-TB were analysed thematically (Flick 2009:24). This section, methodology and research design will be expanded in detail in chapter 3.

1.16 Ethical considerations

Research ethics refers to the system of moral values that are concerned with the degree to which the research procedures adhere to professional, legal and social obligations for the study participants (Council for International Organizations of Medical Sciences (CIOMS 2016:1-2). The researcher received ethical approval to conduct this study from the Department of Health Studies Research Committee at the University of South Africa. The researcher was granted permission by the management team of the study sites to conduct the study. The researcher assured the management team of the study sites of ensuring confidentiality and anonymity of the participants. The involvement of study participants in this study and access to the patients' records was in line with the recommendations of international ethical guidelines (CIOMS 2008:16-28). The objectives of the study, including its aims, benefits and significance were

explained to the participants. Participation was entirely voluntary and participants were free to withdraw from participating in the study at any time. They were informed that a decision not to be part of the study would not have any negative impact on the care and services they obtained from the hospitals.

1.17 Scope and limitations of the study

This study focused only on two referral hospitals in Oromia Region of Ethiopia, Adama Hospital Medical College and Nekemte Referral Hospital. These hospitals and the patients with MDR-TB who attended the same might be different from patients with MDR-TB who attended hospitals in other regions of Ethiopia. The entire study population was used to collect data for its quantitative component. As regards its qualitative component, purposive sampling was used to identify and recruit participants. The qualitative component of the result was based on the reported experiences of the study participants. This is potentially subject to memory bias. It can also be subject to social desirability bias whereby participants might have told the researcher what they think is good to hear. Thus, the outcomes of this study may be generalized with caution.

1.18 Chapter layout of the rest of the thesis

This thesis is divided into six chapters. The main body of the thesis begins with chapter one and ends with chapter six. The main themes of each of the chapters are briefly described here.

1.18.1 Chapter 1

Chapter 1 presents the overview of the study. It orients readers to the study. It also presents the background and rationale of the study. Chapter 1 also presents the objectives and hypotheses of the study. The paradigmatic, ontological, axiological, epistemological and methodological assumptions of the study are presented in chapter 1. The specific methodological approach and research design used in the study and the ethical requirements of the study are also presented in chapter 1.

1.18.2. Chapter 2

Chapter 2 presents peer reviewed scholarly articles and other academic sources such as books on the subject studied. The review of the literature was informed by a number of factors, such as the aims, objectives, research questions and hypotheses of the study, and the theoretical framework that guided the study.

1.18.3. Chapter 3

Chapter 3 presents a detailed discussion of theories, the methodological procedures and the research design that the researcher adopted to address the aims and objectives of the study. The background of the study, study sites, sources of data, and the research instruments used, considerations in data collection and its management and the ethical issues of conducting the study are also presented in chapter 3.

1.18.4. Chapter 4

In chapter 4, research results and their implications are presented. The results section begins with the introduction and profile of the study participants. Then based on the set objectives of the study, the chapter presents the results and their implications regarding treatment outcomes of patients with MDR-TB and the determinants.

1.18.5. Chapter 5

Through synthesis of the evidence generated from the literature review and the study result, a conceptual model was developed and presented in this chapter. Specific gaps in the current programmatic management of patients with MDR-TB were identified and included in this chapter. Moreover, the impacts of available gaps on the clinical care given for MDR-TB, patient satisfaction and adherence to treatment and patient treatment outcomes were identified and included in this chapter. The chapter also includes description of the components of the conceptual model and its practical application in the programmatic management of patients with MDR-TB.

1.18.6. Chapter 6

In chapter 6, discussions on the major results of the study are made in line with the literature. Interpretations are made on the meanings of the quantitative and qualitative results, the connection between the two with the help of the available body of knowledge as indicated in the literature. In addition, the implications of the results of this study on the current practice in the clinical and programmatic management of MDR-TB in the Oromia Region of Ethiopia are also shown.

1.18.7. Chapter 7

Chapter 7 presents conclusion and the recommendations. The research results on independent predictors of treatment outcomes of patients with MDR-TB and factors determining patients' satisfactions are summarised in chapter 7. This chapter also includes recommendations for programme managers and clinical caregivers on the management and treatment of MDR-TB.

1.18.8. List of references

The various literatures synthesized and used in this study are listed in the section of bibliography. For books, journals and other electronic sources used in this study, the authors and sources are identified and acknowledged both in the body of the thesis and also at the end of the thesis by means of a bibliography. As such, all the sources cited in the body of the thesis are listed alphabetically according to the authors' family names.

1.19 Summary

This chapter sets the scene for enhancing understanding of the ensuring chapters. It offers discussions on a number of key issues of the study. Examples of these include background on factors determining treatment outcomes of patients with MDR-TB, the research problem investigated, the conceptual framework on which the entire study was based, the definition of key concepts, and the methodology and research design of the study. The next chapter is a literature review of the extant literature on tuberculosis, MDR-TB and related topics.

Chapter 2: Literature Reviews

2.1. Introduction

Sumerson (2014:45) defines literature review as the process of presenting a theoretical explanation and empirical evidence regarding the problem under investigation. In any research attempt surveying the existing contemporary literature is key before embarking on the research project (Greenhalgh 2010:16). Thus, a study starts from variables, which are later translated into measurable constructs. These measureable constructs provide general shape and structure for the research (Sumerson 2014:18). Literature review helps the researcher to present empirical evidence to support and challenge the research questions and variables used in the research. The volume of available literature on medicine has grown at an unprecedented rate. Thus, searching for medical literature is as challenging as walking in a jungle. Therefore, searching and obtaining a literature that fits into the information need of a particular research objective need to be considered as a big task for a person pursuing research (Greenhalgh 2010:15). In this study, the literature review is guided by the aims, objectives, the research questions and hypotheses of the study.

2.1.1 The purpose of the literature review

In any study, the literature review plays an important role. First, it helps to bring clarity and focus to the research problem. Second, it helps to broaden the knowledge base of the researcher in his or her research area. Third, the literature review helps to contextualize the research results by comparing the results of the current research with the existing body of knowledge (Kumar 2011:27; Polit & Beck 2012:88).

In this study, the literature review presented an organized summary of the results from books, journals and other documents. The summary of results helped to describe the past and the current state of knowledge regarding tuberculosis and especially drug-resistant tuberculosis (Creswell 2012:105-6). Thus the empirical evidence obtained from various sources helped to gain insight about each of the variables and research questions used in the research. By providing an in-depth analysis of available scholarly sources on the topic of interest, literature reviews provide readers with the opportunity to understand what is being researched and why (Roush 2015:20-21).

2.1.2 The search strategy used in this study

For this study, the researcher searched for all English language studies on drug-resistant tuberculosis. The literature search was guided by the constructs included in the theoretical framework of the study. Resources used in this study were accessed from multiple sources. The researcher searched for relevant resources through the UNISA electronic library access, the Medline, PubMed, PLOS, Open Access, www.thelancet.com and the Google. Peer reviewed scholarly articles were researched for clinical and programmatic management of drug-resistant tuberculosis and on factors determining the treatment outcomes of patients with MDR-TB and factors determining patients' perceived quality of care and patients' satisfaction in the care given for MDR-TB. Furthermore, national programme guidelines of the Ministry of Health of Ethiopia and the Oromia Region of Ethiopia were obtained from National Ministry of Health and the Oromia Region Health Bureau respectively. The key words used for searching included the following:

MDR-TB, treatment outcomes of patients with MDR-TB, determinants of treatment outcomes, perceived quality of care, patient satisfaction.

2.1.3 Date delimitation for the literature review

Except for historical analysis of tuberculosis, the date delimitations of the articles and books used in this study focused on those published from 2011 to the present. Some articles and books used from those published before 2011 were for the purpose of describing the historical overview of MDR-TB and the global trend in the response to the problem.

2.1.4 Methodology used in reviewing the literature

The literature was reviewed based on the key themes relevant to the study topic. These key themes are presented in the theoretical framework of the study. As much literature as available on the topic under investigation was surveyed. To make sure that each article is relevant to the purpose of the study, each article was critically appraised using a checklist. Then all relevant and peer reviewed literatures were selected, organized, synthesized and discussed in relation to the study topic.

2.2. The basics of tuberculosis

Tuberculosis (TB) is a chronic infectious disease caused by the bacteria Mycobacterium Tuberculosis. This disease is rarely caused by the other species of the Mycobacterium tuberculosis complex including the Mycobacterium bovis and the Mycobacterium africanum (Heemskerk, Caws, Marais & Farra 2015:1). The Mycobacterium genus is taxonomically located in the Mycobacteriacea family. This genus comprises about 150 species of the mycobacteria (Ozcaglara, Shabbeera, Vandenbergc, Yenera & Bennetta 2012:77). Among members of the Mycobacterium tuberculosis complex, the Mycobacterium tuberculosis has paramount importance in terms of human disease (McHugh 2013:15).

The Mycobacterium tuberculosis is an oxygen-seeking organism. It grows most successfully in tissues with high oxygen content such as the apices of the human lung. The Mycobacterium tuberculosis attacks the host inducing transmission by leading the host to its own self destruction. The Mycobacterium tuberculosis is an intracellular pathogen, usually infecting cells of the immune system, which helps it to hide from the body's defense mechanism.

The Mycobacterium tuberculosis is a slow-growing bacterium. The generation time of 12 to 18 hours for the Mycobacterium tuberculosis is by far longer than that of the 20-30 minutes for other common human bacterial pathogen like the Escherichia Coli (Adams et al 2015:122-23). This makes it a challenge to grow the Mycobacterium in culture media. Rather than having a culture result in two to three days, it can take two to twelve weeks for the Mycobacterium tuberculosis to grow. The Mycobacterium is called acid-fast bacteria due to its staining property (Pálfi, Dutour, Perrin, Sola & Zink 2015:2). This entails the use of special reagents to detect the Mycobacterium tuberculosis (Caminero 2013:14).

Tuberculosis can affect almost any organ of the human body. Nevertheless, 80 percent of all cases of tuberculosis worldwide are pulmonary (Ribon 2015:45-46). Extra-pulmonary tuberculosis (EPTB) occurs in less than 20% of the total tuberculosis cases. The most common forms of the extra-pulmonary tuberculosis are tuberculosis of the

lymph nodes (tuberculosis lymphadenitis) and tuberculosis of the bones (osteoarticular tuberculosis, also known as Potts Disease when it affects the spine). The other form of extra pulmonary parts of the body affected by tuberculosis include the meninges, the intestine, peritoneum and the like (Babatunde, Elegbede, Ayodele, Fadare, Isinjaye, Ibirongbe & Kinyandenu 2013:2010). A person with tuberculosis classically presents as very thin, pale, feverish, and has a cough that produces bloody sputum. If not treated, up to two thirds of tuberculosis patients die of the disease (Bynum 2012:12).

Tuberculosis spreads through airborne transmission. When a person with infectious pulmonary tuberculosis coughs, sneezes, sings, or laughs, small infectious respiratory droplets are aerosolized and released into the airspace. These infectious droplet nuclei may only contain a few of the Mycobacterium tuberculosis bacilli, but a person needs to inhale only a few of these aerosolized droplets to be infected. Droplet nuclei can stay in the air for up to eight hours (Dye 2015:4). A dark room, over crowdedness, and poorly ventilated living quarters, create the perfect environment for tuberculosis transmission. In such an environment, one untreated person with infectious pulmonary tuberculosis, infects an average of ten to fifteen people in a year time (Adams et al (2015:123). The risk of acquiring tuberculosis infection is essentially determined by exogenous factors. These factors are largely social and economic in nature, including substance abuse, chronic illnesses like diabetes and HIV/AIDS, malnutrition and air pollution (Glaziou, Sismanidis, Floyd & Raviglione 2015:5; Heemskerk, Caws, Marais & Farra 2015:9).

Naturally, the Mycobacterium tuberculosis is resistant to cold temperature with the capacity to remain viable for weeks at 4 degrees Celsius. Moreover, due to its high lipid content, the bacterium is also resistant to chemical decontaminations with chemicals like sodium hydroxide or detergents (Caminero 2013:14). However, sunlight kills the Mycobacterium tuberculosis and good ventilation ensure that the droplet nuclei are dispersed and carried outside (Davies et al 2014:131). Unfortunately sunlight and ventilation do not exist in all places. Thus, persons living in confined conditions like the

miners and prison inmates, suffer from high transmission of tuberculosis including drug-resistant tuberculosis. In this way, it is easy to guess how tuberculosis can be easily transmitted from person to person among the more than 10 million people currently living in prisons globally (Fazel & Baillargeon 2011:959). Despite the continuous effort for millennia, tuberculosis has not come under control (Kaufmann 2011:3).

2.3. The basics of multidrug-resistant tuberculosis

Multidrug-resistant tuberculosis is the strain of tuberculosis bacilli that is resistant to the two most potent first-line anti-tuberculosis drugs, i.e. isoniazid and rifampicin (Caminero, Sotgiu, Zumla & Migliori 2010:621; Dheda et al 2014:321). The re-emergence of tuberculosis as a global public health threat is associated with the emergence of multidrug-resistant strains of tuberculosis (Pálfi et al 2015:1; Sullivan & Amor 2013:373; Udwadia 2012:286; Migliori, Cantis, Lange, Richardson & Sotgiu 2010:171).

There is no difference between susceptible tuberculosis and drug-resistance in terms of their ways of transmission and clinical presentation. Moreover, the two strains could not be differentiated based on the results of smear microscopy and radiographic features (Scardigli & Caminero 2013:209). Nevertheless, MDR-TB is a serious public health problem (Nathanson, Nunn, Uplekar, Floyd, Jaramillo, Lönnroth, Weil & Raviglione 2010:1050; Zai, Haroon & Mehmood 2010:279-283). The development of MDR-TB, highly affects the diagnosis and clinical management of tuberculosis as well as patient monitoring parameters. Moreover, it highly compromises the effectiveness of the treatment given for tuberculosis (Caminero 2013:39-44; Vishakha & Sanjay 2013:57). MDR-TB does not respond to the standard six month tuberculosis treatment with first-line anti-tuberculosis drugs. Treatment of MDR-TB can take up to two years or more with second-line drugs. Moreover, second-line anti-tuberculosis drugs are less potent, more toxic and much more expensive than first-line anti-tuberculosis drugs (WHO 2011:1).

Currently, the combination of poverty, HIV/AIDS and drug resistance makes tuberculosis a challenging disease for many people. Moreover, the political and cultural

conditions and stigma associated with the disease determine the occurrence of MDR-TB. Factors associated with the performance of the health system determine patients' access to diagnosis and treatment services for the disease. The combination of these factors affects the outcomes of patients with MDR-TB (Davies et al 2014:3-4).

2.4. Spectrum of drug-resistance in the Mycobacterium tuberculosis

A strain of tuberculosis that is resistant to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-tuberculosis drugs is called rifampicin resistant (RR) tuberculosis (WHO 2014b:18; WHO 2013a:5). MDR-TB is that level of resistance with in-vitro resistance to the two most potent first-line anti-tuberculosis medications - isoniazid and rifampicin (Hatfull et al 2014:413). Moreover, there is a more resistant form of drug resistance called the extensively drug-resistant tuberculosis (XDR-TB). XDR-TB is defined as strains of Mycobacterium tuberculosis with in-vitro resistance not only to isoniazid and rifampicin but also to other classes of medications that comprise the backbone of the regimen used to treat MDR-TB, that is the injectables and fluoroquinolones (Behera 2012:190).

Finally, there is the extremely or totally drug-resistant case of tuberculosis (TDR-TB). Extremely or totally drug-resistant tuberculosis (TDR-TB) is defined as stains of the Mycobacterium tuberculosis that shows in-vitro resistance to all first and second-line anti-tuberculosis drugs tested (Dheda et al 2014:321). The naming of drug-resistance level beyond XDR-TB is not endorsed by the WHO, but it is provisionally named by researchers as 'totally drug-resistant tuberculosis' (Ribon 2015:31; Sullivan et al 2013:373; Tadolini et al 2012:105). The development of TDR-TB signifies the medical and public health urgency associated with drug-resistant tuberculosis (Velayati, Farnia & Masjedi 2013:307).

2.5. Risk factors for development of drug-resistant tuberculosis

Basically, bacteria achieve resistance to drugs through the naturally occurring spontaneous chromosomal mutations at sites of key drug targets. Then it is through the selection pressure that clinically significant drug-resistant bacteria are developed through time (Davies, Gordon & Davies 2014:46-8). There are two principal pathways leading to the development of drug-resistant tuberculosis in an individual. The first of these is the acquired drug resistance. This results from inadequate, incomplete treatment or treatment with poor quality of drugs that allow the selection of resistant strains (Laxminarayan, Duse, Wattal, Zaidi, Wertheim, Sumpradit, Vlieghe, Hara, Gould, Goossens, Greko, So, Bigdeli, Tomson, Woodhouse, Ombaka, Peralta, Qamar, Mir, Kariuki, Bhutta, Coates, Bergstrom, Wright, Brown & Cars.2013:1057-8).

The second type is transmission of drug resistance from patients to healthy persons. The second type occurs in a person who is infected with a drug-resistant strain of tuberculosis. There is synergy between the two forms of drug-resistance in maintaining the continued transmission of the disease in the community (WHO 2014b:7).

2.5.1. Clinical risk factors for the development of drug-resistant tuberculosis

The dominant factor for the development of MDR-TB is the use of suboptimal drug doses and drugs of poor quality, which cause selection pressure and provide a competitive advantage for naturally mutated strains of the bacteria. Furthermore, poor patient adherence to the standard treatment contributes to the development of drug resistance (Dheda, Gumbo, Gandhi, Murray, Theron, Udwadia, Migliori & Warren 2014:332-3; WHO 2014b:107; .McHugh 2013:95; Monedero & Caminero 2010:118-19).

Moreover, there is individual risk factor for development of MDR-TB. These include, young age, male sex, a history of incarceration, infection with HIV/AIDS, a history of previous admission to hospital, alcohol and substance misuse, diabetes mellitus and (Tadesse 2015:65; Dheda et al 2014:324; Gomes, Correia, Mendonça & Duarte 2014:111;Migliori, Sotgiu, D'Ambrosio, Centis, Lange, Bothamley, Cirillo, Lorenzo, Guenther, Kliiman, Muetterlein, Spinu, Villar, Zellweger, Sandgren, Huitric & Manissero 2012:619). Moreover, migration from high MDR-TB prevalent countries has been

identified as the strongest risk factor for MDR-TB (Caminero 2013:43; Miglioria et al 2010:172; Davies, Barnes & Gordon 2008:375).

2.5.2. Programmatic risk factors for the development of drug-resistant tuberculosis

Management of MDR-TB is new for most of the national tuberculosis programmes. As a result, the likelihood of clinical and programmatic errors in managing MDR-TB is high (Monedero & Caminero 2013:3-6; Migliori & Sotgiu 2012:955; Nathanson et al 2010:1050). Moreover, management of MDR-TB is highly demanding in terms of economic and human resources. So far, small proportion of the estimated MDR-TB is detected by the national tuberculosis programmes (WHO 2016:66; Migliori & Sotgiu 2012:955; Zumla, Abubakar, Raviglione, Hoelscher, Ditiu, Mchugh, Squire, Cox, Ford, McNerney, Marais, Grobusch, Lawn, Migliori, Mwaba, O'Grady, Pletschette, Ramsay, Chakaya, Schito, Swaminathan, Memish, Maeurer & Atun 2012:S228; Nathanson et al 2010:1050). Furthermore, the small number of detected cases of MDR-TB are not treated as per the international recommendations (WHO 2014b:10-11; Parsons, SomoskÖvi, Gutierrez, Lee, Paramasivan, Abimiku, Spector, Roscigno & Nkengasong 2011:317-20). This is because resource constraint countries encounter problems in implementing standared recommendations on the clinical management and prevention of the disease (Ortblad, Salomon, Bärnighausen & Atun 2015:2356; Siroka, Ponce and Lönnroth 2015).

2.5.3 The risk of drug-resistant tuberculosis among contacts

Households and close contacts of known patients with MDR-TB are at a higher risk of contracting MDR-TB (Yates, Khan, Knight, Taylor, McHugh, Lipman, White, Cohen, Cobelens, Wood, Moore & Abubakar 2016:233; Caminero 2013:49-50; Seddon, Warren, Enarson, Beyers & Schaaf 2012:1343-44). A retrospective study conducted in Lima, Peru, indicated that 3% of the contacts of MDR-TB patients had active tuberculosis by the time the index MDR-TB case began treatment (Becerra, Appleton, Franke, Chalco, Arteaga & Bayona 2011:147). Yet, due to the absence of rapid, point-of-care testing to identify latent and active tuberculosis the large scale implementation

of active tuberculosis case finding among contacts remains low (Getahun & Raviglione 2010:1206). Children and immunocompromised persons are at increased risk of getting MDR-TB if they come into close contact with infectious cases. Each year there are nearly two million child contacts for each adult drug-resistant tuberculosis source case. In the absence of effective preventive therapy, many of these children go on to develop MDR-TB. (Seddon, Hesseling, Finlayson, Fielding, Cox, Hughes, Faussett & Schaaf 2013:1677). Therefore, it is crucial to actively search for active tuberculosis among close contacts of infectious cases (Erkens, Kamphorst, Abubakar, Bothamley, Chemtob, Haase, Migliori, Rieder, Zellweger & Lange 2010:925).

2.6. Epidemiology of M(X)DR-TB

By 2011, MDR-TB accounted for 3.7 % of new and 20% of previously treated cases of tuberculosis (Zumla, Kim, Maeurer & Schito 2013:285; Scardigli & Caminero 2013:208). In 2013, 9% of the total global tuberculosis cases had MDR-TB. As such, a total of about 480,000 cases and about 210,000 MDR-TB related deaths occurred (WHO 2015:2; WHO 2014a:70). About 5 - 10% of the MDR-TB cases were thought to be extensively drug-resistant (XDR) tuberculosis (Ghanashyam 2016:1149; Pietersen, Ignatius, Streicher, Mastrapa, Padanilam, Pooran, Badri, Lesosky, Helden, Sirgel, Warren & Dheda 2014:123).

There is limited surveillance data in approximately 50% of the high MDR-TB burden countries. Thus, there is a high probability of underestimations in determining the national incidence of MDR-TB (Kumar & Abubakar 2015:s37). By the end of 2012, 84 countries had ever reported at least one case of extensively drug-resistant tuberculosis (Günther 2014:283; Harding, Foley, Connor & Jaramillo 2012.643). Currently, a combination of factors is contributing to the development and spread of MDR-TB globally. These factors include substance use, prevalence of co-morbidities like HIV and diabetes mellitus, malnutrition, incarcerations, overcrowding, migration, income inequality, and the cultural, political and religious factors around the community at risk of the disease (WHO 2014b:132).

In general, the prevalence of drug-resistance is lower in sub-Saharan African countries but it is higher in the countries of the former Soviet Union and China (Raviglione 2010:128). In the Russian Federation and some neighbouring countries, up to 18% of new cases of tuberculosis are multidrug-resistant (The Institute of Medicine 2012:30). Most African countries are also hard hit by the epidemic of drug-resistant tuberculosis. South Africa has about 18% of the global burden of laboratory-confirmed cases of MDR tuberculosis and the highest number of confirmed cases of XDR-TB (O'Donnell & Schluger 2014:1193-94). As such, it shares 87.9% of the African burden of MDR-TB (Biadglegne, Sack & Rodloff 2014:3). Furthermore, 97.6% of the total 2,336 XDR-TB patients reported from five African countries were from South Africa. In Somalia, the proportion of MDR-TB cases among cases of pulmonary tuberculosis was 7.7% (Sindani, Fitzpatrick, Falzon, Suleiman, Arube & Adam et al 2013:479).

2.7. Epidemiology of drug-resistant tuberculosis in Ethiopia

Ethiopia is among countries with high burden for MDR-TB. In 2011, there were an estimated 2200 (1300-3200) cases of MDR-TB in Ethiopia. Of this number, only 212 (9.6%) were detected and only 199 (9%) of those detected were enrolled for MDR-TB treatment (Falzon, Jaramillo, Wares, Zignol, Floyed & Raviglione 2013:690). Moreover, the annual incidence of MDR-TB cases in Ethiopia for the year 2011 was estimated at 2,200 (1300-3200). But the number of MDR-TB cases ever detected and enrolled for MDR-TB treatment in the country has been far below the annual incidence estimate. In 2008, there were a total of approximately 5200 MDR-TB cases in Ethiopia and only 130 (2.5%) were notified by the national tuberculosis programme (Falzon et al 2013:691).

2.8. Challenges associated with M(X)-DR-TB

2.8.1. Diagnostic challenges associated with M(X)-DR-TB

Until recently, the diagnosis of tuberculosis was largely based on the 130-year-old smear microscopy technique and remains the cornerstone for the diagnosis of tuberculosis (McHugh 2013:1-10). However, the technique has limitations that are particularly associated with its low sensitivity (Tadolini, Centis, D'Ambrosio & Migliori 2012:102).

It worth noting that, the sputum smear microscopy cannot be used to identify strains of tuberculosis that are resistant to anti-tuberculosis drugs. The culture of the Mycobacterium tuberculosis followed by drug susceptibility test are needed for the diagnosis of MDR-TB (Kirwan & Gilman 2012: 103). Thus, diagnosis of MDR-TB requires implementation of sophisticated biosafety practices and equipment to prevent inadvertent infection of laboratory personnel (Minion & Pai 2010:941).

In many resource limited countries, the high cost and the technical complexity associated with culture and drug susceptibility testing precludes its routine use in clinical diagnosis of tuberculosis. Furthermore, it takes weeks to months for culture results to be available for clinical decision making. This leads to delays in the diagnosis of patients suffering from strains of tuberculosis resistant to first-line drugs which in turn lead to treatment of MDR-TB cases with inappropriate regimen, leading to the further amplification of resistance (Dobler, Korver, Batbayar, Nyamdulam, Oyuntsetseg, Tsolmon, Surmaajav, Bayarjargal & Marais 2015:1451). Besides, culture is technically demanding, expensive and also not widely available (Scardigli et al 2013:208; WHO 2012a:27-28).

2.8.2. Clinical and programmatic challenges associated with M(X)DR-TB

Clinical management of MDR-TB is challenging both for patients and clinicians. Its treatment is complex, expensive and needs a long treatment period (at least two years). Drugs used to treat MDR-TB are expensive, toxic and less effective. Also, specific expertise is needed to provide a comprehensive service and care for patients with the disease and for the management of drug related adverse events. Furthermore, the treatment outcome of drug-resistant tuberculosis is generally poor (that is low treatment success rate) (Sotigu & Migliori 2014:364-365). As a result, multidrug-

resistant and extensively drug-resistant tuberculosis are becoming a major health challenge since the second half of the 20th century (Wallis 2013:106). Globalization, health inequalities, competing economic interests and political instability substantially contribute to the development and spread of drug-resistant tuberculosis (Lange et al 2014:23).

2.8.3. The socio-economic challenges associated with MDR-TB

The high incidence of tuberculosis is an indicator of poverty, healthcare inequalities and hardships like migration (Lange et al 2012:194). As such, the association between tuberculosis and socio-economic development is an insight that should be acted upon today. The continued global challenge due to tuberculosis and MDR-TB is largely attributable to the failure in how human society is structured and functions than from failure of medical practice (Benatar & Upshur 2010:1215-1217).

A study conducted in India indicated that the poor are five times as likely to have tuberculosis as the rich (Institute of Medicine 2012:7-8). Acknowledging this, poverty affects patient treatment behaviours and their adherence with medical advice and adherence to treatment. Therefore, in many different settings, patient incentive and treatment enablers have been shown to improve patient adherence with medical advice and their adherence to treatment (Adams et al 2015:129).

2.9. Clinical management of multidrug-resistant tuberculosis

2.9.1. Standard approaches to the management of MDR-TB

The treatment of multidrug-resistant or extensively drug-resistant tuberculosis is mainly bio-medically oriented. This means that a combination of second-line anti-tuberculosis drugs are used to treat the disease (Dooley, Obuku, Durakovic, Belitsky, Mitnick & Nuermberger 2013:1352). Second-line drugs are categorized into five groups according to their perceived potency and the role they play in the regimens used to treat M(X) DR-TB. When some of these second-line drugs are believed to have useful efficacy, the efficacy of others (such as amoxicillin‑clavulanic, rifabutin) are queried because they are many others associated with significant toxicities. Second-line drug toxicity affects the tolerability of the regimen by the patient (Davies, Gordon & Davies 2014:233).

Surgery as an adjuvant treatment for M(X)DR-TB may help treatment of MDR-TB if certain clinical criteria are met. Surgery may be considered as an adjuvant intervention to chemotherapy when four likely effective second-line drugs are not available and the lesion is localized so that there is sufficient respiratory reserve. Surgery is likely to have good impact in the case of XDR-TB where pharmacological options are extremely limited. When indicated, surgical intervention is recommended at the time of lowest bacillary load, ideally after sputum conversion (Scardigli et al 2013:213).

Resection surgery as an adjuvant intervention to chemotherapy has been proved to be effective and safe under appropriate surgical conditions. Yet the procedure needs skilled thoracic surgeons and excellent post-operative care. Timing of surgical intervention is recommended to be earlier in the course of the disease when the infection is local. The M/XDR-TB patient needs to be on treatment for at least two months prior to considering surgical intervention.

Adjuvant treatment to chemotherapy is required for certain patients with M/XDR-TB. Corticosteroids have the potential to affect the body's response to fight tuberculosis; their use should be based on clear clinical indication. Nutrition and micronutrient supplementation are part of the standard management of M(X)-DR tuberculosis (WHO 2014b:93-4).

2.9.2. Standard registration groups for MDR-TB

Cases of drug-resistant tuberculosis are registered based on a previous treatment history (that is the outcome of the latest tuberculosis treatment). In this way, patients are registered under two broad categories of registration groups (new and previously treated). A patient is new if he or she hasn't ever received anti- tuberculosis treatment or received anti-tuberculosis treatment for less than 1 month. Patients in the previously treated group include the relapse, treatment after failure and treatment after lost to follow ups. A case of relapse tuberculosis patient is one in which previous tuberculosis treatment was successfully completed and the patient was subsequently diagnosed of tuberculosis (Federal Ministry of Health of Ethiopia 2014:45). Patients with tuberculosis

who after taking anti- tuberculosis for more than one month become lost to follow ups for two months or more time and then return to treatment with active tuberculosis, are registered as 'treatment after lost to follow ups'. Treatment after failure is that group of patients who remain sputum or culture positive at five month or longer after commencing the treatment for tuberculosis. There are also some groups of patients with tuberculosis who are registered under the 'other previously treated' group of patients. These patients are those who have previously been treated for tuberculosis but whose most recent tuberculosis treatment outcome is not known or not documented. Based on their HIV sero-status, patients may be registered in the HIV positive or HIV negative group of patients (WHO 2013a:4).

2.9.3. Clinical and laboratory monitoring scheme for patients with MDR-TB

Prior to initiation of treatment with second-line anti- tuberculosis drugs, all diagnosed patients with MDR-TB undergo baseline clinical and laboratory tests. These include detailed clinical, serological, bacteriological and radiological evaluations. In that case, thyroid, hepatic and renal function tests and complete blood counts are done. The tests also include voluntary counselling and testing for HIV (Sanjay 2013:53).

Once the patient is initiated on treatment, routine laboratory monitoring of the treatment process and its outcome is considered to be one of the five components of the global Directly Observed Treatment Short Course (DOTS) strategy. The Directly Observed Treatment Short Course also remains as a core element in the global Stop TB Strategy. Currently, routine monitoring of the patients' sputum and culture conversion is the main method to assess the response to treatment of the patients with MDR-TB. For patients with MDR-TB, laboratory results help to make clinical decisions including determining the duration of chemotherapy (Glaziou et al 2015:8).

Clinical symptoms and radiographies are used to assess the status of patients' response to treatment. In the case of patients with MDR-TB, smear conversion has less predictive value than the culture for monitoring patients' response to treatment. Thus, even though it is too demanding, culture is a better parameter for monitoring patients' response to treatment (Caminero 2013:43).

It is recommended that patients with MDR-TB be closely monitored for their response to chemotherapy. For this, close laboratory monitoring helps to promptly pick up signs of treatment failure and drug-toxicities. Additionally, regular history taking, physical examination, laboratory tests and chest radiology are crucial for patients treated for MDR-TB. The conversion of sputum culture to negative is the most sensitive criteria for assessing improvement. The conversion of sputum smear microscopy to negative is important for monitoring the patient's response to treatment mainly because of its shorter turnaround time. Yet sputum culture is most sensitive to detect the response to treatment (WHO 2014b:139-40).

2.9.4. Standard treatment outcome options for patients with M(X) DR-TB

In the same way as standard registration groups for patients with MDR-TB, there are standardized definitions to assign treatment outcomes to patients with M(X)DR-TB. As such, there are about six standard definitions for outcomes of MDR-TB treatment (WHO 2013a:6). Thus, a patient with MDR-TB patient is given one of these six outcome definitions, mainly based on available data on results of laboratory and clinical follow up services. The six standards MDR-TB treatment outcome options include cured, treatment completed, treatment failed, died, lost to follow up and not evaluated. In the definition of treatment outcome, the term 'treatment success rate' implies the sum of patients with MDR-TB those who are cured and those who completed treatment (Federal Ministry of Health of Ethiopia 2014:47; WHO 2014b:18).

2.10. Factors determining the clinical management & the treatment outcomes of patients with MDR-TB

2.10.1. Socio-demographic determinants of the treatment outcomes of patients with MDR-TB

Tuberculosis affects all ages and both sexes. In 1988, while in prison, Nelson Mandela, was diagnosed with tuberculosis after presenting with pleural effusion and he received treatment for tuberculosis (O'Donnell & Schluger 2014:1193).

There is complex interaction between patients' socio-demographic factors and the management of patients with MDR-TB. Lack of education, unemployment and distance from health facility are associated with an increased risk of treatment interruption by patients with MDR-TB. Personal factors like smoking, drug and alcohol use, co-infection with HIV and perceived severity of illness are risk factors for treatment interruption (Ndwandwe, Mahomed, Lutge & Knight 2014:56). Older age and the use of alcohol are associated with the increased risk of hepatotoxicity among patients treated for MDR-TB (WHO 2014b: 85; Caminero 2013:123). Being a male patient, inadequate knowledge of tuberculosis and the need for treatment adherence, and stigma may affect patients' adherence to treatment (Muture, Keraka, Kimuu, Kabiru, Ombeka & Oguya. 2011:2). Male patients with tuberculosis are at a higher risk of treatment non-adherence than women. Men's breadwinner status as head of households explained their lower adherences to treatment (HerreroI, RamosI & ArrossiI 2015:295). In Nigeria, patients who live more than five kilometers away from treatment centres, lack of knowledge on the duration of tuberculosis treatment and cigarette smoking were associated with treatment interruption (Anyaike, Musa, Tunde, Bolarinwa, Durowade & Ajayi 2013:1441).

2.10.2. The socio-economic determinants of the treatment outcomes of patients with MDR-TB

Tuberculosis is mainly a social disease that inequitably affects the poor in resource constrained regions of the world (Schaaf & Zumla 2009:19). The poor, lack access to the basic life resources like food, water and sanitation, and therefore poor lack control over their lives (Benatar & Upshur 2010:1215-6).

Poverty related factors such as poor living conditions and under nutrition, increase the likelihood of infection by tuberculosis and its subsequent progression to an active disease (Rusen, Squire & Billo 2011:163). Poverty and food insecurity are both causes and consequences of tuberculosis. Poverty enhances the transmission of tuberculosis (Peltzer & Louw 2014:157). Most of the world's high-burden tuberculosis countries such as Ethiopia and Kenya are poor and have a high level of unemployment. In these countries, tuberculosis is aggravated by poverty. It contributes to unemployment and lack of adequate nutrition. Poor nutrition, on the other hand, is a risk factor for the development of tuberculosis (Schaaf et al 2009:605).

Patients with tuberculosis face the double burden of reduced income and increased expense. As patients are often too weak to work, their families are obliged to pay for the medical expenses needed in seeking diagnosis and treatment for the disease. Patients and their families encounter indirect costs related to travel costs and lost income due to the disease and its treatment (WHO 2013b:10). In Armenia, the poor economic status among patients with tuberculosis is associated with an increased chance of default from treatment (Sanchez-Padilla, Marquer, Kalon, Qayyum, Hayrapetyan, Varaine, Bastard & Bonnet 2014: 160). In Georgia, the low monthly household income and unemployment were predictors of poor treatment outcomes among patients with MDR-TB (Djibuti, Mirvelashvili, Makharashvili & Magee 2014:1). Among the poor patients with MDR-TB, malnutrition was associated with a low cure rate and a high rate of death. It was evident that economically weak patients who lead a poor lifestyle are unable to continue with the lengthy MDR-TB treatment. Such patients do not appreciate the need to continue treatment once they feel improved

(Vishakha & Sanjay 2013:57). Therefore, for the poor patient provision of tuberculosis medications that are free of charge alone are not effective. Because tuberculosis is associated with indirect expenses and lost income, it impedes the poor patient's adherence to care. Thus, increasing funding on interventions that target social determinants of tuberculosis is crucial to ensure the successful management of patients with tuberculosis (Siroka, Ponce & Lönnroth 2015:5).

Thus, patients with tuberculosis need social and financial support that enables them to complete their treatment. It must be acknowledged that the availability of social support improves patients' treatment outcomes (Basili, Fitzpatrick, Qadeer, Fatima, Yloyd & Jaramillo 2013: 278).

2.10.3. The MDR-TB drug regimen as a determinant factor for the treatment outcomes of patients with MDR-TB

There are two requirements in the approach to the management of drug resistant tuberculosis. The first is the need to use multiple drugs to avoid further resistance. The second is the need to treat the patient for a sufficient duration of time in order to kill the dormant bacilli and prevent relapse (Monedero & Caminero 2010:120).

Currently, treatment for MDR-TB is given for at least 20 months. The recommendation for such a long treatment duration is based on very poor quality evidence. The available supporting data has not been able to provide information on whether the duration of the intensive phase and time of sputum conversion can influence the patient's clinical outcomes (Scardigli & Caminero 2013:212-213).

The lengthy MDR-TB treatment regimen currently in use is often poorly tolerated by patients. It is also difficult to monitor it (Van Deun, Maug, Salim, Das, Sarker, Daru & Rieder 2010: 684). In addition, optimal drug regimens for MDR-TB are poorly characterized. There are no fixed dose combination tablets and so patients are required to take many tablets per day. This makes patients' adherence to treatment a major challenge during the lengthy treatment period (Zumla et al 2012:S234).

It is apparent that the multiple anti-tuberculosis drug regimens used for the management of MDR-TB can be standardized or individualized regimens. It is suggested that standardized regimes are useful in settings with high MDR-TB burden

and low skilled physicians. This is because standardization facilitates prescription and the approach to patient management. Individualized regimens are preferred in patients with previous exposure to second-line drugs and for patients with XDR-TB who failed on the standard regimes (Scardigli & Caminero 2010:212).

Compared with settings that use the individualized MDR-TB treatment regimen that is guided by laboratory drug-sensitivity test results and local drug-susceptibility patterns, settings using standardized or empiric treatment regimens under programmatic conditions, report poorer treatment outcomes in terms of treatment success. It was found that the favourable treatment outcomes of patients treated with individualized regimen is 10% more than the treatment outcome of patients treated with standardized regimen (64% for individualized vs 54% for standardized regimen) (Zumla et al 2012:S234). Analysis of the treatment outcomes of 204 culture confirmed patients with MDR-TB in the United Kingdom has shown that the type of second-line drugs used determine the level of treatment outcomes. Furthermore, patients who are treated with regimen containing fluoroquinolones or a bacteriostatic drug are more likely to have a successful treatment outcome compared to those who did not. (Anderson, Tamne, Watson, Cohen, Mitnick, Brown, Drobniewski & Abubakar 2013:406).

2.10.4. Factors related to the MDR-TB disease

An individual patient with MDR-TB may be infected by mixed strains of the Mycobacterium tuberculosis termed as phenotypic drug sensitivity test heterogeneity. The presence of at least a tuberculosis bacilli that is susceptible to rifampicin and isoniazid in culture isolates, indicates the presence of an infection with a heterogeneous strain. Infection with mixed heterogenic strains of tuberculosis is a risk factor for unsuccessful treatment outcome. Compared with patients without phenotypic heterogeneity, patients infected with heterogenic strains are at greater risk of poor clinical outcomes (Zetola, Modongo, Moonan, Ncube, Matlhagela, Sepako, Collman & Bisson 2014:1760).

In tuberculosis and HIV co-infected patients', the presence of heterogenetic strains delays culture conversion and prolongs the chance of disease transmission (Zumla et al 2012:S234). Similarly, the severity of the MDR-TB determines the clinical management of MDR-TB. The presence of severe forms of MDR-TB, including bilateral and extensive lung lesions and high initial bacillary load, are associated with poor treatment outcomes (Vishakha & Sanjay 2013:54). Granulomatous lung lesions, for example, are poorly vascularized and are difficult to access with anti-tuberculosis drugs (Hichey 2016: 260). Retreatment or re-treating is a predictor of treatment failure, death and default among patients with tuberculosis (Peltzer & Louw 2014:157).

2.10.5. Adverse drug reactions from second-line drugs

Adverse drug reactions are common among patients with MDR-TB who are treated for the disease (Akshata, Chakrabarthy, Swapna, Buggi & Somashekar 2015:27; Blasi, Barnes, Gaga & Migliori 2013:1). Seventy two (72) out of the 73 patients treated with second-line drugs in Addis Ababa, Ethiopia, encountered at least two adverse drug reactions in the course of their treatment (Bezu et al 2014:147). From a cohort of 63 patients with MDR-TB, those treated at the LG Hospital-Ahmedabad, 36 (57.14%) of the patients experienced second-line anti-tuberculosis drugs related adverse reactions of varying severity (Vishakha & Sanjay 2013:55).

An analysis of second-line drug related adverse drug reactions among 1027 patients with MDR-TB in Latvia, indicated that adverse drug reactions from second-line drugs are prevalent. The study revealed that, 79% of patients experienced at least one type of second-line drug related Adverse drug reactions with a median of three adverse drug reaction events per case (Bloss, Kukša, Holtz, Riekstina, Skrip ˇconoka, Kammerer & Leimane 2010:275). It has been observed that adverse drug reactions lead to treatment interruption before completion. As such, it contributes to morbidity, treatment failure, reduced quality of life or death (WHO 2014b:35-6). In Armenia, poor treatment tolerance because of adverse drug reactions is associated with an increased risk of default from treatment and poor patient response to treatment (Sanchez-Padilla et al 2014: 164).

There are many risk factors for the occurrence of adverse drug reactions. These include the presence of co-morbidities that demand the simultaneous use of several drugs. Factors related to the patient's condition like being very young or very old age, allergy to drugs, pregnancy, breast feeding and diseases that alter drug metabolism and its elimination from the body increase the likelihood of adverse drug reactions (WHO 2012b:65).

For example, the use of fluoroquinolones in patients with low body weight is associated with more adverse drug reactions. Also, there is a risk of hypoglycemia associated with the use of gatifloxacin in elderly patients (Caminero 2010:624).

About 25-45% of patients treated with Linezolid reported severe anemia with or without thrombocytopenia or peripheral and optic neuropathy. It has also been noted that bacteriostatic second-line drugs like para-amino salicylic acid and Ethionamide are major causes of hypothyroidism (Caminero 2013:141; Caminero 2010:627). Moreover, the sodium salt formulations of para-amino salicylic acid (PAS) cause sodium retention resulting in excessive sodium load in the body which should be avoided in patients with renal insufficiency (WHO 2014b:112-13). Both Linezolid and/or Rifabutin anti-tuberculosis medications have been associated with myelosuppression, anemia, neutropenia, peripheral and optical neuropathy. Thioacetazone is associated with high toxicity in patients with HIV co-infection (Caminero et al 2010:627). The other common adverse reactions from second-line drugs is loss of hearing (Seddon, Faussett, Jacobs, Ebrahim, Hesseling & Schaaf 2012:1277-83).

In conclusion, adverse drug reactions should be anticipated, promptly identified and treated to avoid defaulting from treatment due to drug side effects (D'Ambrosio, Tadolini, Centis, Duarte, Sotgiu, Aliberti, Dara & Migliori 2015:158-159; Blasi, Dara, van der Werf & Migliori 2013:493; Caminero et al 2010:621-29; Monedero et al 2010:123).

2.10.6. Co-morbid conditions affecting the management of MDR-TB

There are overlapping comorbidities between tuberculosis and other diseases. Co-morbidities with MDR-TB have one thing in common, that is, they all reduce the host immune response to tuberculosis. HIV, malignancies, diabetes mellitus, and chronic renal failure are the best examples (Raviglione 2010:98-9). If a patient with MDR-TB is immunocompromised, the tuberculosis bacilli resists the phagosomes-lysosome fusion by which the bacteria is naturally killed. Thus, the bacilli can continue to multiply (Hichey 2016: 260). As such, the presence of diseases like HIV/AIDS, diabetes mellitus, and renal and liver disease affect the process and outcomes of the treatment given for MDR-TB (Marais, Lönnroth, Lawn, Migliori, Mwaba, Glaziou, Bates, Colagiuri, Zijenah, Swaminathan, Memish, Pletschette, Hoelscher, Abubakar, Hasan, Zafar, Pantaleo, Craig, Kim, Maeurer, Schito & Zumla 2013:436).

In the United Kingdom, 26.7% of the total 204 culture confirmed patients with MDR-TB diagnosed between 2004 and 2007 had a co-morbidity with MDR-TB. About 54.4% of the patients had at least one change to their treatment regimen at some point during the course of their treatment. The study showed that patients who have any co-morbidity with MDR-TB are more at risk of death ($p<0.0005$). Specifically, co-infection with HIV is associated with risk of death ($p<0.0005$) followed by co-infection with diabetes mellitus ($p=0.002$) and chronic renal disease ($p=0.002$) (Anderson et al 2013:406). It is evident that HIV fuels the occurrence of tuberculosis and is a risk factor for the development of MDR-TB. A survey of patients with MDR-TB conducted in Ukraine indicated that HIV infection is an independent risk factor for the development of MDR-TB (Ayles & Godfrey-Faussett 2009:1450). Also, the HIV pandemic and the rising trend of MDR-TB in sub-Saharan Africa form a synergistic impact on treatment outcomes of drug-resistant tuberculosis. There are indications that a high degree of immunosuppression and drug-resistance are associated with poor treatment outcomes of patients with MDR-TB (Gandhi, Andrews, Brust, Montreuil, Weissman, Heo, Moll, Friedl & Shah 2012:90). Co-infection with HIV is associated with poor treatment outcome and high mortality among both patients treated for susceptible tuberculosis and MDR-TB (Babatunde et al 2013:213).

The presence of any co-morbidity with MDR-TB therefore necessitates the concomitant use of other medications. This increases the risk of drug interactions and overlapping drug toxicities (WHO 2014b:85). Additionally, the extraordinary high pill burden that MDR-TB and HIV co-infected patients take needs special attention. Note that these treatments could amount to more than 30 tablets per day (Caminero 2013:172). A greater degree of immunosuppression, usually very low T-lymphocyte cell bearing (CD4) count, and a high level of resistance to anti-tuberculosis drugs, are associated with a greater risk of death (Gandhi, Andrews, Brust, Montreuil, Weissman, Heo, Moll, Friedland & Shah 2012:90). Thus, earlier initiation of anti-retroviral therapy is recommended for tuberculosis and HIV co-infected patients. This recommendation encompasses even those patients severely immune-compromised. A study conducted in Ethiopia on 512 patients, revealed that a better chance of survival was observed among patients with T-lymphocyte cell bearing (CD4) count of 50 cells/µl or less who were initiated on anti-retroviral therapy as early as 1 week (Naidooa, Baxtera & Abdool Karim 2013:2-7).

There is a further documented link between diabetes mellitus, smoking, alcoholism, chronic lung diseases, cancer, immunosuppressive treatment, malnutrition and tuberculosis. Diabetes mellitus is the most common co-morbidity both in MDR-TB and XDR-TB (14.5% for MDR-TB) and 15.4% for XDR-TB) (Yuan, Zhang, Kawakami, Zhu, Zheng & Li et al 2013:1). Malnutrition is one of the co-morbid conditions presenting with clinical tuberculosis. Malnutrition is not only a risk factor for the development of tuberculosis but it also occurs as a consequence of infection with tuberculosis. In addition, it is also associated with gastro-intestinal disorders and mal-absorption. Also, the Low Body Mass Index (BMI) and lack of adequate weight gain are associated with death and the relapse of tuberculosis. Thus, malnutrition, as a co-morbid condition, is an indication of the disease severity and poor patient response to treatment (WHO 2013b:8). In conclusion, addressing co-morbidities presenting with tuberculosis is crucial for improving patient response to tuberculosis treatment. In fact, the management of co-morbidities with MDR-TB should be considered as part of the

comprehensive and standard of care for tuberculosis. This entails an integrated management and care for tuberculosis and other co-morbidities. The aim of such an approach will be to improve the general health and quality of the life of patients treated for M(X)DR-TB (WHO 2013b:7).

2.10.7. The effect of malnutrition on the management of MDR-TB and its treatment outcomes

Tuberculosis, like other infections, increases energy requirements by the body. The presence of malnutrition with tuberculosis is an indication of disease severity. Low body mass index (<18.5kg/m^2) and lack of adequate weight gain in the course of tuberculosis treatment are associated with poor response to treatment and a higher risk of death (WHO 2013b:8). Protein energy malnutrition is the most common form of malnutrition among patients with MDR-TB. Protein energy malnutrition and specific nutrient deficiencies debilitate the cell-mediated immune system, which is important in the protection against tuberculosis. Once tuberculosis develops, it induces a catabolic state resulting in negative nitrogen balance and micronutrient deficiencies (Cegielski & Vernon 2015:490). As a result of poor conditions, protein energy malnutrition affects those people living in poverty, the elderly and young children and is common in people affected by infectious diseases like tuberculosis and HIV/AIDS. Tuberculosis and HIV/AIDS not only depletes body proteins, but they also demand extra energy. It is observed that these diseases induce nutrient loss and alter metabolic pathways (Whitney & Rolfes 2008:197). For people suffering from tuberculosis, poor nutrition intake worsens pre-existing malnutrition and impairs recovery (Caminero 2013:201).

MDR-TB causes malnutrition and the second-line drugs given to treat it decrease appetite and exacerbate pre-existing malnutrition. Patients suffering from borderline hunger can also be enmeshed in a vicious cycle of malnutrition and disease (Caminero 2013:142). Therefore, anti-tuberculosis treatment may not be fully effective if the problem of malnutrition is not addressed. So, provision of free food during MDR-TB treatment improves the patients' weight and the quality of their lives (WHO 2014b:94). Hence, the recommendation is for adequate nutrition support, including vitamin

supplementation like vitamin B6 should be provided for patients on MDR-TB treatment (Lange et al 2014:44). Vitamins and minerals supplementation and adjuvant therapies to alleviate symptoms of pain are important interventions for patients on MDR-TB treatment (WHO 2014b:93-94). Patients with MDR-TB should be provided with free food. Provision of free food should therefore not be considered as an incentive but should rather be seen as a necessary intervention to facilitate treatment success for MDR-TB. It has been proved that nutrition intervention improves the body's response to treatment and increases chances of patient survival (Caminero 2013: 201). In this way, tuberculosis and especially MDR-TB is more than a medical problem (Monedero & Caminero 2013:7). A focus only on drug-regimens needed to treat MDR-TB is therefore insufficient in the absence of strong social support. It seems obvious that spending thousands of dollars on expensive second-line drugs makes no sense if patients default from treatment because of hunger (Monedero & Caminero 2010:123). On top of the abovementioned interventions, continuous patient counselling and follow up support are critical to improve the quality of the patients' life and the safety of other people living around the patient with MDR-TB (Zai et al 2010:279).

2.10.8. Cost of illness associated with MDR-TB

Tuberculosis causes catastrophic health expenditure (defined as direct health expenditures corresponding to 40% of the annual discretionary income) during the pre-diagnosis and pre-treatment period. As most of the expenditure occurs before the patient is diagnosed with tuberculosis, minimizing treatment cost in the course of treatment does not guarantee financial risk (Tanimura, Jaramillo, Weil, Raviglione & LÖnnroth 2014:1770) especially because patients with tuberculosis still encounter financial risk during treatment. In Swaziland, transport cost and user fees for registration at health facilities are among factors that limit patients' access to care (Sanchez-Padilla, Dlamini, Ascorra, Rüsch-Gerdes, Tefera and Calain, Tour, Jochims, Richter & Bonnet 2012:35). In Argentina, the burden of transportation costs and the type of health facility where patients get treatment for tuberculosis are major explanatory factors of patients' adherence to treatment. Patients with tuberculosis that are employed and are also getting social protection had higher levels of treatment

adherence than those patients with employment but with no social protection (HerreroI et al 2015:295).

For patients with tuberculosis is around half of their annual income (Burki 2015:21). In some settings, patients with MDR-TB and their families spend over half of their annual income due to tuberculosis. About 60% of this cost is due to days off work and out of pocket expenditure (Ortblad et al 2015:2356). Even when treatment is free, patients face a high financial burden during their attendance to treatment (Arakawa et al 2011:1000). Costs incurred by patients and their families include direct medical expenses, travel costs and lost income due to illness. In Nigeria, the cost incurred due to tuberculosis is 37% of the median annual household income (Ukwaja, Alobu, lgwenyi & Hopewell 2013:1). In China, the poorest are disproportionately affected by tuberculosis. Excluding the income losses due to the disease, the direct out-of-pocket expenditure due to tuberculosis is 55.5% of the average annual household income. Thus, the family falls into heavy debt. In Tanzania, 68–98% of tuberculosis related costs incurred by patients and their families is associated with patients' loss of income related to reduced capacity to work. Therefore, families are forced to sell productive assets or are forced into migrant labour (Jackson, Sleigh, Wang & Liu 2006:1104). In Ethiopia, the annual cost incurred by TB-HIV co-infected patients and their family is documented to range from 49% to 71% of the annual household income (Vassall, Seme, Compernolle & Meheus 2010:604).

The greater economic burden borne by MDR-TB is associated with its total duration of illness. Compared to the average of 12 months from symptom onset to end of treatment for susceptible tuberculosis, the average total of 40 months from symptom onset to end of treatment for MDR-TB is much longer. This indicates that the high economic burden imposed by tuberculosis on patients and their families is much greater than the average annual household income (Rouzier, Oxlade, Verduga, Gresely & Menzies 2010:1316). In Equador, the total per capita MDR-TB related cost was found to be US$ 6880, which is 223% of the average Ecuadorian annual income (Vassall, Seme, Compernolle & Meheus 2010:604). As a result, some cases of depression among MDR-TB patients

are associated with socio-economic problems rather that due to the drugs used to treat MDR-TB (IUATLD 2010:129-30). In this way, tuberculosis is described as a driver of poverty, a condition that causes perpetuation of the disease. Tuberculosis and especially TB-HIV co-infected patients face loss of employment, reduced income, stigma and discrimination. They also face gender violence and family separation. On the other hand, these patients require additional resources to achieve good treatment results. Thus if patients with tuberculosis are made to pay for diagnosis and or treatment, their chance to delay seeking medical service or interrupt treatment is very high (Caminero 2013:142).

2.10.9. Model of treatment delivery as a factor determining MDR-TB treatment outcomes

One of the key components of the Directly Observed Treatment Short Course (DOTS) Strategy is the direct observation of the tuberculosis treatment. Direct observation of every dose of anti-tuberculosis drugs is effective in making sure that each daily dose of anti-tuberculosis drugs is taken by the patient (Caminero 2013:164). In order to achieve a cure, it is of utmost importance to ensure that the patient takes all the daily drugs according to medical instructions. Thus, treatment must be administered by a trained treatment supporter (preferably health caregivers) who will observe the patient taking all doses of prescribed drugs under direct observation (Lange et al 2014:37). Introduction of the direct observation of treatment for MDR-TB, has enabled dealing with the increasing number of drug-resistant tuberculosis (The Institute of Medicine (IOM) 2012:22).

Yet from the perspective of the patient with MDR-TB, there are many important concerns that impair their adherence to the ideal treatment under daily Directly Observed Treatment support (Caminero 2013:192-193).

Available evidence estimates that up to 60 percent of patients with chronic disorders, poorly adhere to treatment (Robinson, Gould & Strosahl 2010:87). It is documented that as many as 50% of patients with tuberculosis miss an occasional appointment for medication. Thus, the acceptable tuberculosis treatment process and its optimum treatment outcome depend on the continued commitment of the patient and particularly

of the healthcare workers to ensure a high level of adherence to standard medical advice (Bosworth, Oddone & Weinberger 2006:147). For a patient who is treated for a clinically established diagnosis and using drugs of established efficacy, adherence to treatment may be established by following certain ethical approaches. The patient should get ongoing treatment support and the patient's interest regarding the treatment, should be respected. Patients should be able to comfortably discuss any problem when it arises to minimize chances of treatment interruption (Bosworth, Oddone & Weinberger 2006:13).

However, the daily observed treatment approach is interpreted differently by patients in different settings. According to a studies conducted in South Africa and Vietnam, patients interpret daily observed treatment as a sign of patient distrust (Arnadottir & Iceland 2009:679-82). Distance from the treatment centre and economic barriers are risk factors for non-adherence to treatment Therefore, reduced distance between the patients' home and the facility where tuberculosis treatment is given reduces the cost of round-trip transportation. As such, it is noted that patients treated at primarily health facilities have better adherence and treatment outcome (Herrero, Ramos & Arrossi 2015:287; Loveday, Wallengren, Brust, Roberts, Voce, Margot, Ngozo, Master, Cassell & Padayatchi 2015:167; Alobu, Oshi, SN, Oshi, DC & Ukwaja 2014:782-3). Community-based models of MDR-TB management help to reduce the cost of illness and improve treatment outcomes (Scardigli & Caminero 2013:214).

Yet, decentralized care model requires strong coordination between health professionals at formal health facilities and community level social workers (Heller, Lessells, Wallrauch, Bärnighausen, Cooke, Mhlongo, Master & Newell 2010: 423). The Institute of Medicine (IOM) states two things that are of priority concern in the decentralization of Daily Observed Treatment support for patients with MDR-TB who are treated with second-line drugs. The first of these concerns is that, if second-line drugs are given erratically without strict supervision and especially with doses that are not correct, more severe forms of drug-resistance like extreme and total drug-resistant tuberculosis can develop. The second concern is the issue of disease transmission if the household level infection control is not strong (The Institute of Medicine 2012: 17, 39).

Moreover, the choice of a treatment supporter by the patient and the willingness of treatment supporters to take on the responsibility for the Daily Observed Treatment support is another challenge on the effectiveness of daily observed treatment. An overworked and poorly paid healthcare worker may not be motivated to take responsibility for Daily Observed Treatment. Such practical issues make the usefulness of the Daily Observed Treatment strategies to be questionable in the long run. Furthermore, laypersons other than family members, are sometimes rejected by the patient usually relating to the issue of confidentiality (Arnadottir et al 2009:682).

Nevertheless, every patient with MDR-TB who is linked to outpatient and community based treatment support, needs to have a dedicated worker as a single point of contact for any challenge he/she faces in the course of treatment. Additionally, there should be a system whereby patients are regularly appointed to hospitals for follow-up adherence support and for scheduled clinical assessment. Moreover, facilities initiating treatment should be responsible for contact investigations and the assignment of the appropriate treatment outcome upon treatment completion by the patient (Lange et al 2014:45).

2.11. Factors determining patients' perceived quality of care and patient satisfaction with care given for MDR-TB

2.11.1. Factors related to the health service quality

Quality is elusive, means that, it is difficult to define. Quality is context-dependent and multidimensional (Kajonius & Kazemi 2015:2). According to Avedis Donabedian (2005:691) "the definition of quality may be almost anything anyone wishes it to be, although it is, ordinarily, a reflection of values and goals current in the medical care system and in the larger society of which it is a part" (Donabedian 2005:691-2). The Institute of Medicine defines quality in the context of health services. In this way, quality is the degree to which a health service is meant to serve individuals and populations and increase the likelihood of desired health outcomes also consistent with contemporary professional knowledge (Višnjić, Veličković & Jović 2012: 54).

There is a definition of quality put forward by Donabedian. He defines health service quality in terms of technical and interpersonal quality. Technical quality stresses that

the desired health outcome of procedures, tests and services that the patient receives sufficiently exceeds anticipated health risks. The second segment of the Donabedian aspect of quality, that is, interpersonal quality, argues that all patients are treated in a humane and culturally appropriate manner and they are also part of the decision made regarding the services they take. The other aspects of quality include content (service) quality. There is also an ethical dimension of quality that focuses on the need for health services to be safe, effective and patient-centred (Donabedian 1988:1743).

2.11.2. Dimensions of the health service quality

Quality of care can be decomposed into three distinct but interrelated components. These are structure, process and outcome. Structural quality includes factors that affect the conditions in which the care occurs. Structural quality also includes parameters like resources, the number and the training level of the staff who provide care for patients. Structure encompasses factors like the payment methods and the availability of basic facilities and equipment in the premises in which care is provided. The second component of quality, that is, process quality is related to how the caregiver behaves towards patients, whether the patient is treated with respect and is involved in the treatment decision making process. Outcome measures of quality focus on changes in the patient's health status, behaviour and satisfaction. These three dimensions of quality affect patients' perception of quality of care and their satisfaction (Kajonius & Kazemi 2015:1-2). Thus the measurement of the quality of healthcare entails the assessment of structural variables like the setting in which the services are given and the characteristics of caregivers. It also entails assessing what service givers do to their patients and caregivers' adherence to service standards and recommendations. It also entails measuring the effect of the treatment received. That is, what happens to patients or including changes in their perception of the quality of the services they received and their satisfaction with care they received (Longest 2015: 237-244).

Patient-centredness of healthcare is one of the main measures of quality. The 1998 conference held at Salzburg, Austria, developed a self-described vision for a patient-

centred health care system. According to this vision, there are certain characteristics of a patient-centred healthcare. These characteristics include that the care is easily accessible to the patient, the patient takes part in the care decision making process and the patient is well informed of the care he or she receives. It also entails that the care is provided through a well-coordinated care team so that the patient is given integrated comprehensive care. In addition, routine feedback from the patient, leads to practice improvement and lastly there is information that enables the patient to choose a caregiver that meets his or her service needs (Davis, Schoenbaum & Audet 2005:953-4). Patient-centredness of healthcare can also be measured, based on six dimensions of patient-centredness of services. These dimensions advocate for the fact that the care must be respectful to patients' values, preferences, and expressed needs.

2.11.3. The effect of health care quality on patients' perceived quality of care and their satisfaction

The level of interaction between caregivers and patients and whether patients and their surrogates get the necessary information, determine the level of understanding about the services that the patient gets and the patients' perceived quality of care, patient's adherence to medical advice and their overall satisfaction (Bosworth, Oddone & Weinberger 2006:329). Quality of health communication between patients and their caregivers is one important measure of quality of care. Communication between the patients and their caregivers is an art and a technique of informing, influencing, motivating and engaging individuals towards achieving a desired common health outcome. Health communication helps to create meaning in relation to the physical, mental and social wellbeing of individuals and enhance their quality of life in the community. Caregiver-patient communication is required in the patient's best interest and towards arriving at restoring the patient's health or relieve the patient's suffering (Harrington 2015:9-10). Barriers to effective patient-caregiver communication are the patients' anxiety, doctors' burden of work, fear of physical or verbal abuse and unrealistic patient expectations (Fong Ha & Longnecker 2010:39). Health communication is fundamentally interpersonal regardless of the setting. Interpersonal communication refers to the interactions between two individuals who know each other

and share common goals (Slonim & Pollack 2005:264-7). Communication can be verbal or non-verbal. Thus, caregivers need to be conscious of the implications, rewards or risks associated with any communication that they make with their patients. In relation to tuberculosis treatment, low patient awareness about tuberculosis and unpleasant staff behaviour, determine patient satisfaction with care given. Similarly, long waiting hours for a service, drug related side effects and the lengthy treatment period for MDR-TB negatively impacts the process and outcome of MDR-TB treatment (Zai et al 2010:280-2).

Equally important, is that patients are actively involved in the decision made regarding the care and services they receive. Moreover, care and services given are well coordinated and integrated, and also that patients get appropriate information, communication, and education. This ensures physical comfort and provides emotional support for patients (Pagano 2015:1-2). In this regard, patient-reported data is a reliable means of measuring the patient-centredness of the healthcare service (Slonim & Pollack 2005:267; Tzelepis, Sanson-Fisher, CZucca & Fradgley 2015:831).

2.11.4. Factors determining patient adherence to MDR-TB treatment

A meta-analytic study of all published empirical literature from 1948 through 1998 using different samples and measurement techniques, has revealed that one out of every four patients leaves do not adhere to treatment. In the case of patients with MDR-TB, the presence of social support and a passionate behaviour of the health caregivers promote patients' adherence to treatment. On the other hand, adverse drug reactions, poor communication with caregivers, lack of food, stigma, pill burden and economic constraints negatively affect patient adherence to treatment (Gebremariam, Bjune & Frich 2010:1-7). An individual's action or lack of action to change his or her behaviour results from the evaluation of several constructs. The patient's adherence to treatment is determined by interplay of multiple factors. These factors include the type of the disease, beliefs and expectations of patients and their perceived disease severity and its curability. The complexity of the treatment regimen and the socio-cultural factors

around the patient are factors determining patient adherence to treatment (Fertman & Allensworth 2010:346-7).

2.11.5. The effect of communication between patients and their caregivers on patients' adherence to treatment

According to the information-motivation strategy model, people fail to adhere to treatment recommendations due to three level factors. Firstly, people may not understand what they are supposed to do. This is associated with poor communication between patients and their caregivers. Secondly, patients may not be motivated to carry out recommended actions. Lack of motivation may be associated with lack of belief in the efficacy of the treatment and the resultant negative attitude towards it. Thirdly, patients may not have workable strategies to accomplish treatment recommendations as they face practical barriers in their lives (Martin & DiMatteo 2014:10-13). According to the theory of social learning, the majority of re-inforcers of human behaviour are social in nature including acceptance and smiles. The cognitive aspect of learning behaviour is influenced by outcome expectancies (or response efficacy). According to the cognitive social learning theory, the expectancy that a positive outcome or consequence will occur is a function of behaviour (Bosworth, Oddone & Weinberger 2006:13). If patients with MDR-TB feel well and if the behaviour of the caregivers is unfriendly, patients with MDR-TB are more likely to interrupt treatment (Ibrahim, Hadejia, Nguku, Dankoli, Waziri, Akhimien, Ogiri, Oyemakinde, Dalhatu, Nwanyanwu & Nsubuga 2014:1). Therefore, caregivers need to be polite, kind and responsive to the care needs of patients with MDR-TB (Dheda et al 2014:326). Good communication between caregivers and the patients helps to increase treatment adherence. Effective caregiver–patient communication can improve adherence by:

- Increasing patient knowledge and understanding,
- Changing patient beliefs and attitudes, and
- Increasing patient motivation by encouraging patients to actively participate in their healthcare (Bosworth, Oddone & Weinberger 2006:330).

Tuberculosis is predominately a disease of socially vulnerable groups. This makes adherence to the extended course of tuberculosis treatment a considerable challenge. Thus, ensuring patients' adherence to tuberculosis treatment is a major programmatic challenge in many settings (Kaliakbarova, Pak, Zhaksylykova, Raimova, Temerbekova & van den Hof 2013:62). Without effective strategies to ensure patient adherence, the chance for further development of drug resistance will increase among patients with MDR-TB. The World Health Organization recommends that non-adherence to standard tuberculosis treatment should be less than 5% (HerreroI et al 2015:288).

2.11.6. The effect of the duration of treatment on patient adherence

At the outset of the lengthy MDR-TB treatment period, it is difficult to predict the patients' adherence to treatment. The lengthy time needed for the completion of MDR-TB treatment exhausts patients' financial and practical abilities. It also exhausts patients' families to provide the continued support needed to complete treatment (Maswanganyi, Lebese, Mashau & Khoza 2014:2). Compared with patients who are treated for a short period of time, patients treated for a longer period are at an increased risk of an unfavourable treatment outcome (Ukwaja, Oshi, Alobu & Oshi DC 2016:122-3). In the case of patients with tuberculosis who live in remote rural areas of China, the cost of transport to meet the scheduled facility visits imposes a high economic burden and affects adherence to treatment. Some patients move from one place to another without reporting to the treatment supporter and they end up discontinuing treatment. Besides, patients with tuberculosis who experience adverse effects from anti-tuberculosis drugs cannot complete their treatment (Zhao, Wang, Tao & Xu 2013:6).

2.11.7. The effect of performance of the healthcare system on patients' satisfaction

Patient satisfaction is indicative of the health system's performance. The quality of healthcare given by a healthcare setting is the major determinant factor of client satisfaction, client retention and their adherence to medical advice. In turn, the clients' perception of the quality of healthcare is affected by multiple factors. These factors are related to the hospital environment and the demographic as well as socio-economic characteristics of clients (Brahmbhatt, Baser & Joshi 2011:27-28). Patients' judgement or perception on the quality of healthcare that he or she receives determine patients' satisfaction (Donabedian 1988:1746). A satisfied patient does not present with formal complaints and does not go into initiating malpractices. Moreover, a satisfied patient benefits the doctor in terms of job satisfaction, reduced stress and less burn-out (Fong Ha & Longnecker 2010:39).

2.11.8. The effect of healthcare quality on patient satisfaction

In the course of the management of MDR-TB, patient satisfaction with healthcare is among the major factors that determine the management and the clinical outcome of the disease (Punnakitikashem, Buavaraporn, Maluesri & Leelartapin 2012:1232; Menedero et al 2010:124). As it is to be expected, optimum adherence to treatment prevents treatment failure, relapse and development of further drug-resistance. As such, when good adherence to treatment contributes to better MDR-TB treatment outcome, poor adherence to treatment leads to the development of acquired forms of drug resistance like the extensively drug-resistant tuberculosis (Zai et al 2010:279; Dheda et al 2014:326).

It has been noted that there is a positive relationship between the quality of healthcare provided and patient satisfaction. Understanding the patients' perception of quality of the clinical services given and their satisfaction with the care they receive is important for hospital managers and doctors. It helps them to identify points of strength and weakness and gear the care given for the patient towards the preferences of patients. As such, it helps to work towards improving the quality of the services given and patient satisfaction overtime (Ramez 2012:132-139).

Patients with MDR-TB must receive ongoing counselling and support. This is because sub-optimal patient adherence to treatment leads to the further development of drug-resistance and would render patients practically untreatable (Ferguson & Rhoads 2009:607). During the lengthy and toxic treatment period, interventions that improve patient satisfaction are essential for patients on treatment. These include the provision of comprehensive psychosocial and economic support, including nutritional support.

The condition of treatment set-ups and the availability of patient-centred care are other factors determining client satisfaction and their adherence to treatment (Caminero 2013:202). The availability of an appropriate treatment environment such as supportive accommodation with access to continuous counselling and palliative care, improves patient satisfaction and promotes patient adherence to treatment (Cox, Hughes, Ford & London 2012:178).

2.11.9. The effects of stigma on patients with MDR-TB on patient's satisfaction

The word stigma is derived from the Greek meaning "a mark or a stain". Stigmatisation is a complex and dynamic process of devaluation of individuals that significantly discredits the individual in the eyes of others. Within particular cultures or settings, certain attributes are seized upon and defined by others as discreditable or unworthy. When stigma is acted upon, the result is discrimination that may take the form of actions or omissions (Stop TB Partnership 2015:12). A study conducted in Urban Zambia, revealed that 82% of patients with tuberculosis reported some form of stigma associated with tuberculosis. The study indicated that the consequences of stigmatisation similarly prevailed among children and adults with tuberculosis. The consequences of the stigmatisation included low self-esteem, insults, ridicule, discrimination, social exclusion and isolation, resulting in the decreased quality of patients' life and social status (Cremers, de Laat, Kapata, Gerrets, Klipstein-Grobusch & Grobusch 2015:2).

In case a control study conducted in Sudan, both cases and controls (who had tuberculosis) reported the presence of a mild level of tuberculosis related stigma. The

study revealed that a higher TB related stigma was observed among the older, unemployed patients and those living in rural areas. Thus, the study concluded that the TB related stigma impaired the quality of life of tuberculosis patients due to concerns about disclosure, effects on work, education, marriage and family life (Suleiman, Sahal, Sodemann, El Sony & Aro 2013: 390-92). The World Health Organization states that palliative care and issues related to stigma and discrimination are essential components of the comprehensive management of MDR-TB (WHO 2014:66). Patients' psychosocial problems and how the community perceives and interprets tuberculosis, determine how the patient copes with the disease and its treatment (Caminero 2010:47). Hence, the stigma towards patients with tuberculosis is one of the major factors that determine patient adherence to treatment. Therefore, on-going education support is needed for patients with tuberculosis and their families in order to reduce the effect of stigma and to make sure that patients continue treatment for the entire duration of treatment (Lange et al 2014:45).

2.11.10. The role of psychosocial support on patient satisfaction

The MDR-TB treatment has impacts on patients' mental health. This impact is greater among patients with limited social and financial support (Khanal, Elsey, King, Baral, Bhatta & Newell 2017: e0167559-1). The patients' psychological stress, including the perception of illness, affects patients' adherence to treatment. On its own, the perception of illness and illness behavior is affected by the patients' cultural, educational, ethnicity, family structure and socio-economic differences. Very often, patients with tuberculosis suffer from feeling ignored. Usually, patients experience a wide range of psychological reactions including fear, depression and anger (Munsab, Santanu, Ravinder, Pradeep & Ankur 2013:123-125). It has also been observed that patients with MDR-TB sometimes show abnormal behaviour. Such behaviour is often associated with alcohol or substance misuse. The misuse of substance by patients with MDR-TB is associated with repeated default from treatment. Such patients are sometimes difficult to manage in hospitals and will often escape from hospitals and even threaten or assault hospital staff and other patients (Gandhi, Nunn, Dheda, Schaaf, Zignol, Soolingen, Jensen & Bayona 2010:1838). However, the abnormal

behaviour of patients need not be criticized. Rather, it should entail working towards gradually transforming such behaviour so as to restore the individual's function within his or her environment and culture. Working towards enabling patients to regain wellness requires the physician's intervention in such behaviour in various ways. Such intervention includes not only healing the patient's body from prevailing ailments but it also needs addressing the patient's psychosocial problems to facilitate the restoration of the patient's function (Fulford, Davies, Gipps, Graham, Sadler, Stanghellini & Thornton 2013:65).

Currently, the management of MDR-TB is shifted from the predominantly hospitalized model to the outpatient model of care. This entails strong emotional and social support towards improving treatment outcome (Skrahina, Rusovich, Dara, Zhylevich & Hurevich 2014:79). A study conducted in East Kazakhstan region, revealed that patients with MDR-TB suffered from a myriad of social and psychological problems. These include alcoholism, unemployment, very low-income, absence of social support, homelessness, and lack of official documentation that prevented access to the state social support. A programme on psychosocial support for patients with MDR-TB, was aimed at improving treatment adherence for patients at high risk of treatment interruption. This study revealed that there were no defaulters among patients with MDR-TB who were covered in the psychosocial support programme. This study highlighted the importance and the need for psychological counselling and support for patients on treatment (Kaliakbarova et al 2013:60-64). Therefore, understanding problems that patients with MDR-TB face during treatment and the knowledge of patients' perceptions, may help the national tuberculosis programme to take appropriate interventions to alleviate these problems. Ongoing social and psychological support should therefore be an essential element of the national MDR-TB control programme to enhance patients' adherence to treatment. Furthermore, psychosocial support should be available in the context of the outpatient model of MDR-TB treatment. Moreover, the care and services provided should be comfortable for and acceptable by patients with MDR-TB (Lange et al 2014:44).

2.11.11. The effect of service set-ups and the caring practice of caregivers on patient satisfaction

It has also been revealed that the setup of the healthcare organization and the performance of a health system influence the tuberculosis control. This influence lies more in the way the health services are organized to detect and treat tuberculosis than in the rate of tuberculosis case detection and treatment success (Loveday, Padayatchi, Wallengren, Roberts, Brust, Ngozo, Master & Voce 2014:1; Arakawa et al 2011:995). The physical facilities of the service setups, the equipment and appearance of the personnel who provide the service, influence the satisfaction of patients with MDR-TB. Likewise, caregivers' ability to perform the services accurately and dependably affects patients' perception of the quality of care and patient satisfaction with the care and services they receive. Added to this, the degree of caregivers' willingness to attentively assist clients and provide prompt service determines patients' satisfaction with care given. Similarly, other parameters, including caregivers' empathy and assurance, (ability to convey trust and confidence) determine client satisfaction with clinical care (Ramez 2012:132). There is also a correlation between patients' perception of quality of care that they receive at hospitals and the level of their satisfaction. Dimensions like reliability, responsiveness, assurance, empathy, including tangibles, play a pivotal role in determining patients' perceptions of quality and their satisfaction with care given on MDR-TB (Kavitha 2012:157).

2.12. Summary

Guided by the aims, objectives of the study and the theoretical framework of the study, chapter 2 presents the literatures reviewed to explore and understand the available body of knowledge on treatment outcomes of patients with MDR-TB and its determinants. The next chapter, chapter three, presents the philosophical, methodological assumptions and the specific methods that guided the study.

Chapter 3: Research Design and Methods

3.1. Introduction

Research methodology is a subfield of epistemology. It is concerned with the procedures followed in scientific investigations (Babbie 2014:4). It relates to the principles and ideas on which the research procedures and strategies (methods) are based (Holloway & Wheeler 2010:21). In other words, research methodology is a detailed account of exactly what the researcher is going to do or has done. Simply, it tells the readers whether the results of a study are valid and reliable, and serves as the means researchers use to systematically solve research problems (Roush 2015:38).

This chapter discusses the research methodology used in this study. It also describes the study design and the specific research methods or techniques used in this study. It provides a description of the study setting and study population. The chapter encompasses the procedures used for sampling and recruitment of the study participants. It also includes the steps used for the development of the study instrument and the procedures of data collection, and data management or data processing. Procedures used for ensuring the validity, reliability and trustworthiness of the study results, and ethical considerations of the study are also presented in this chapter.

3.2. Study setting and study population

3.2.1. Study setting

Study setting describes the organization or community in which a research endeavour is conducted. It covers the characteristics of the community being studied. This includes the community history, its size, composition and structure. Regarding the organization in which a study is conducted, it encompasses the administrative structure of the organization, and the type of services that the organization provides (Kumar 2011:186). In a nutshell, the research setting is the situation, or environment that surrounds the population or group being studied. Simply, a study setting may be physical locations like organizations or schools. It may also be historical contexts of

the population studied like religion, politics, economy, and the environment in which they live (Creswell 2012:473).

3.2.1.1. Background of Ethiopia

This study was conducted at two sites in the Oromia Region of Ethiopia. Ethiopia is located in the horn of Africa. It lies between 3 and 15 degrees, north latitude and 33 and 48 degrees east longitude. With its total area of about 1.1 million square kilometres, Ethiopia borders Eritrea to the north, Djibouti to the east, Sudan to the west, Kenya to the south and Somalia to the south-east. Its topographical features range from as high as 4620 metres above sea level at Ras Dashen mount to as deep as 110 metres below sea level in the Afar Depression. The Great East African Rift Valley divides the highland of Ethiopia into two (Federal Ministry of Health of Ethiopia 2013:28).

Ethiopia is governed by a federal government called the Federal Democratic Republic of Ethiopia (FDRE). The Federal Democratic Republic of Ethiopia is composed of nine regional states. These are the Afar, Amhara, Benshangul Gumuz, Harari, Gambella, Oromia, Somali, Southern Nations Nationalities and Peoples Region and Tigrai regions. In addition to the nine regional states, Ethiopia has two city administrative councils, which are Addis Ababa and Dire Dawa city administrations. Figure 3.1 below depicts the political map of Ethiopia.

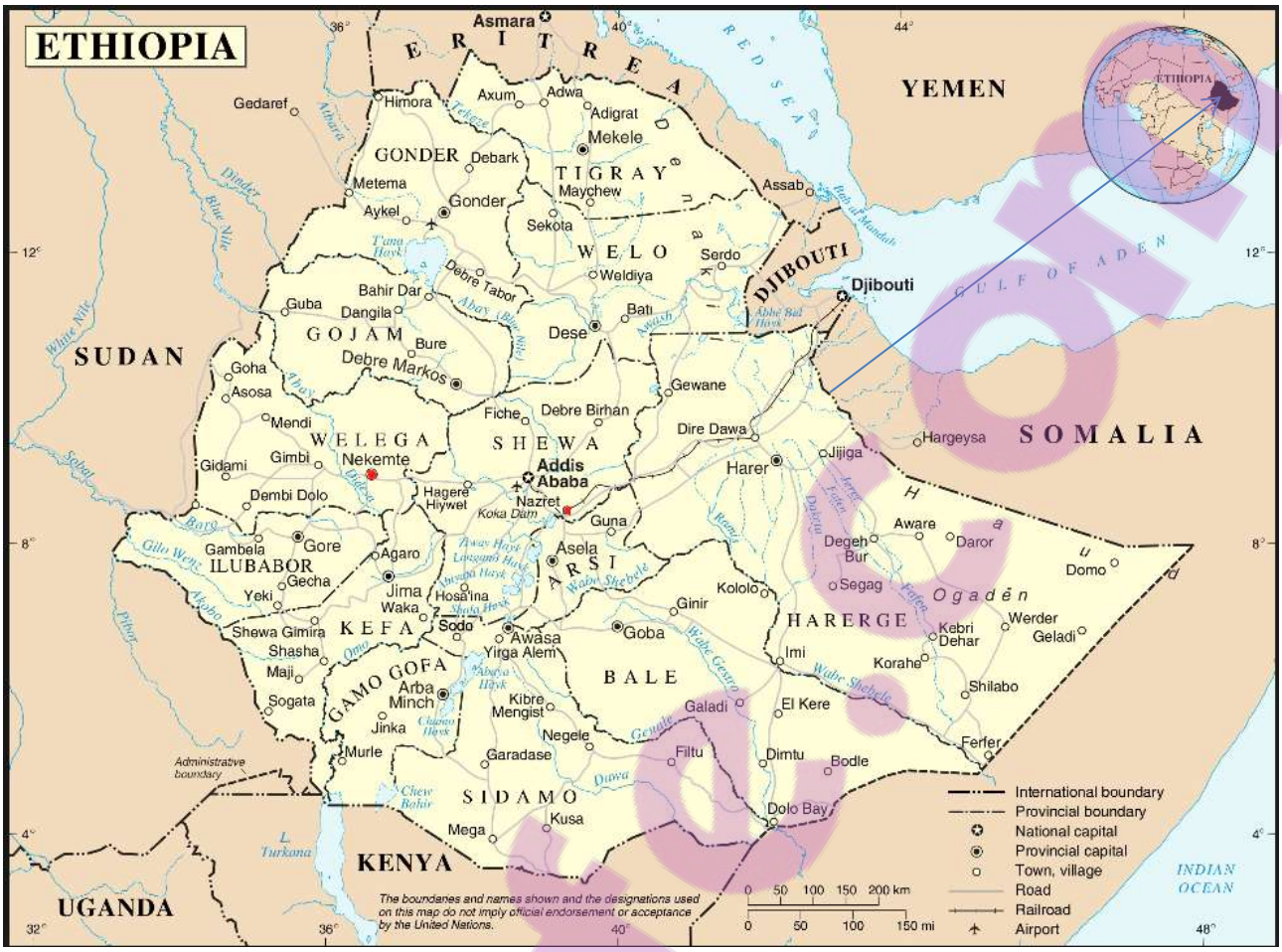


Figure 3. 1: Political map of Ethiopia with provincial/state boundaries (Source: World Trade Press. 2015. Best country reports: Political map of Ethiopia with provincial/state boundaries.

3.2.1.2. The Oromia Regional State of Ethiopia

The Oromia Region is one of the nine regional states of the Federal Democratic Republic of Ethiopia. This region is the biggest of all the regional states in terms of its total population and landmass. According to regional population projection estimates made by the national central statistical agency of Ethiopia, the total population of the Oromia Region for the year 2016 and 2017 was estimated to be 35,875,159. The region covers an area 359,619.8km^2 stretching from the Sudan border in the West up to the Somali regional state of Ethiopia in the East. It borders Kenya in the South.

Administratively, the Oromia region is sub-divided into 38 provincial and 326 district administrative units. The districts are further sub-divided into 7,011 ‘kebeles’ (the

lowest administrative unit in Ethiopia). About 6,521 (93%) of the ‘kebeles’ are rural, while 490 (7%) of them are urban (Oromia Region Health Bureau/ORHB/ 2015:3-4).

Except the Tigrai Region, Oromia Region shares borders with all the other regional states of Ethiopia and the two city administrations of Ethiopia (Central Statistical Agency of Ethiopia 2015:1). Geographically, the Oromia Region of Ethiopia is located centrally and is stretched from East to West of the country. As the Oromia Region shares borders with the majority of the Federal States of Ethiopia, it has patient referral links with all its neighbouring regional states. It was for this reason that the Oromia Region was selected with the assumption that the results of the study would reflect the programmatic management of drug-resistant tuberculosis in the other regions of Ethiopia.

3.2.1.3. Health service coverage of the Oromia Regional State

The Oromia Region Health Bureau (ORHB) is responsible for providing comprehensive health services in the Region of Oromia. The healthcare delivery system of the Oromia Region of Ethiopia aligns with the national three-tier arrangement system for healthcare delivery to the regional populations. The first or basic level in the tier is the primary care level. The primary care level consists of the community health post, which is responsible for providing preventive public health services to a median population of 5,000. It also encompasses a health centre, which is responsible for providing first level preventive and curative healthcare for an average population of 25,000. The primary level also consists of the primary hospital that is responsible for providing inpatient and ambulatory healthcare to a median population of 100,000. The second level in the tier consists of all general hospitals in the country. Each general hospital is responsible for providing curative care and services in all areas of specialties for a median population of one million. The third or tertiary level consists of all specialized hospitals each of which is designed to provide tertiary level care for a median population of five million (Federal Ministry of Health of Ethiopia 2010:74-5).

There are 66 public hospitals, 1,363 government owned health centres and 7,011 health posts in the Oromia Region. Furthermore, there are 2 regional reference laboratories and 7 blood banks to support the quality of diagnosis and clinical care provided by the regional healthcare facilities. There are also private health facilities in the Oromia Region. The private health facilities provide tuberculosis case detection and treatment services in partnership with the government health facilities. Simply, the private health facilities contribute to the regional tuberculosis case detection and treatment.

The regional health care network model implemented in the Oromia Region, notes that health care professionals at health centres are responsible for supporting community health posts within their respective catchment populations. The urban health extension package is supported by the respective and health offices in the towns. The respective health centres and health offices in the towns support the urban health extension package. The primary hospitals are required to support health centres in their catchment areas. The primary hospitals are supported by the general hospitals which in turn are supported by specialized hospitals. In 2014, the health service coverage of the Oromia Region was 97% (Oromia Region Health Bureau (ORHB) 2015:2).

3.3. Study sites

This study was conducted between the 10th of November 2016 and 7th of February 2017 at two referral provincial hospitals located in the Oromia Region of Ethiopia. The two referral hospitals were Adama Hospital Medical College and Nekemte Referral Hospital. Adama hospital medical college is located 98 Km to the east of Addis Ababa while Nekemte Referral hospital is located 328 Km to the west of the capital, Addis Ababa. The two hospitals included in this study were selected based on convenience (Etikan, Musa & Alkassim 2016:4; Crano et al 2015:234; Huck 2012:101). The rationale for selecting the two hospitals was that, given the time and resources at hand, it was not practical to access all hospitals in Ethiopia that provide care to people with MDR-TB.

Adama Hospital Medical College and Nekemte Referral Hospital were the two hospitals in the Oromia Region where programmatic management of drug-resistant tuberculosis was first initiated in 2012 in Ethiopia. As such, these hospitals were selected with the assumption that they have adequate experience and data on programmatic management of drug-resistant tuberculosis in the Oromia region. The selected hospitals are located in Adama and Nekemte towns. They therefore deserve to be described briefly.

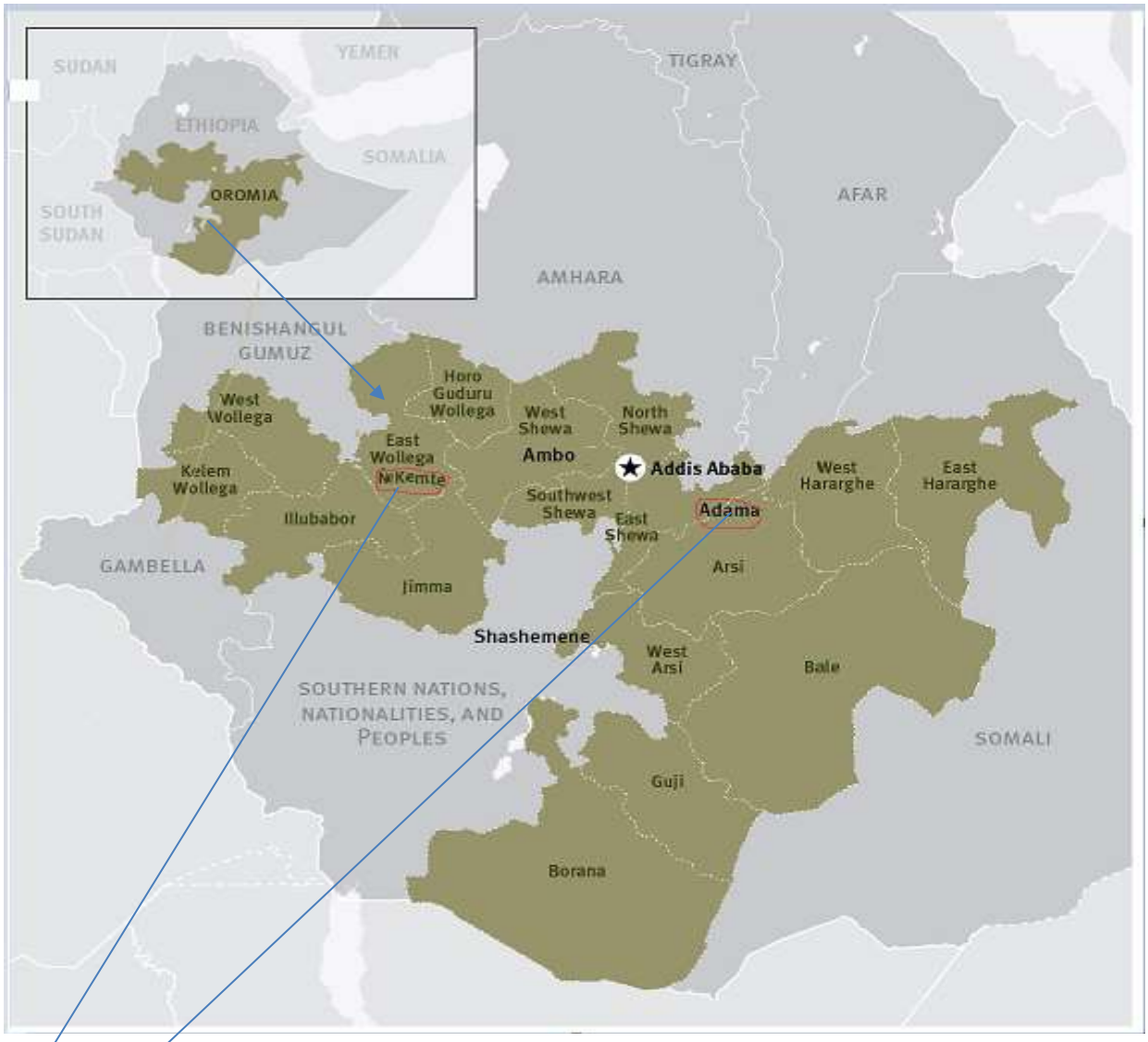


Figure 3. 2: Map of the Oromia Region in Ethiopia (Source: https://www.google.com/search?q=map+of+the+Oromia+region+of+Ethiopia (accessed 14 November 2017).

3.3.1. Adama town

3.3.1.1. Topography, population characteristics and political administration of Adama town

The Adama town was established in 1916. Its establishment aligns with the introduction of the Ethio-Djibouti railway at the time. The town of Adama is located at the distance of 100 kilometres to the South-eastern part of the capital, Addis Ababa. It is on the road that connects the capital with the seaport of Djibouti. Adama is a busy transport centre that connects different regional states to the capital. Administratively, the town of Adama is divided into 8 kebeles (the lowest administrative unit in Ethiopia). The town is located in the Great Rift Valley Region of East Africa (Adama town Health office. 2016:1-2).

Adama is located 8°32′ N 39°16′ E / 8.54°N 39.27°E / 8.54; 39.27 and is situated at an elevation of 1712 metres above sea level. The total landmass of Adama town is estimated at 13,000 hectars (Adama Town Health Office 2016:2). The total population of Adama town for the year 2017, was estimated at 365, 828 (male=181,011 (49.5%) and female=184,818 (50.5%) (CSA-E 2017:1).

3.3.1.2. Health service coverage of Adama town

Currently, Adama town has nine government health centres, 1 government and 5 private hospitals, 71 private clinics and 104 pharmacies. As such, potential health service coverage for the population of Adama town for the year 2017 was 100% (Adama town Health office 2016:2).

3.3.2. Nekemte Town

3.3.2.1. Topography, population characteristics and political administration of Nekemte Town

Nekemte (Oromo: *Naqamtee*, means betrothed) is a market town and one of the administrative towns in the western part of the Oromia Region of Ethiopia. Nekemte town is located in the East Wollega Zone of the Oromia Region. The town has a latitude and longitude of 9°5′N 36°33′E / 9.083°N and 36.550°E / 9.083N; 36.550 respectively and an elevation of 2,088 metres. Nekemte town is one of the historical towns of the Oromia Region. The town has been the capital of the former Wollega province, and is home to the museum of Wollega Oromo culture. Moreover, the Nekemte town is the burial place of Onesimos Nesib, a famous Oromo who translated the Bible to Oromo Language for the first time in collaboration with Aster Ganno. A central government customs office was officially opened in Nekemte in 1905. The town is a host city to the newly built Wollega University as of 2017 (Nekemte Town Health Office 2017:1-2).

The total population of Nekemte town for the year 2017, was estimated at 118,523 with the male proportion equals to 60,484 (51%) and the female proportion equal to 58,040 (49%) (CSA-E 2017:1).

3.3.2.2. Health service coverage of Nekemte town

The Nekemte town has two government owned hospitas (one was opened in 1932), three health centres and many privately owned clinics and speciality centres. The health service coverage for the population of Nekemte town for the year 2017 was 100% (Nekemte Town Health office. 2017:2).

3.4. The research design

This section of chapter three describes the research design adopted for answering the research question of this study. It also covers the rationale for choosing the study's research design.

3.4.1. The research design used in this study

A research design is a master plan that specifies the methods and procedures that can be used for collecting and analysing information or data needed to solve research problems (Pandey & Pandey 2015:18). Research design denotes both a process and a product. Given that there is no one single blueprint for planning research study, research designs are governed by the notion of fitness for purpose. This means that the purpose of a research study is what determines the methodology and the research design that researchers adopt. For a mixed methods design study, like this one, a research design allows the measurement of variables of interest in a particular way (Groat & Wang 2013:24).

This study employed a concurrent mixed methods design (Blaikie 2010:200). This design has two components, quantitative and qualitative (Hesse-Biber & Johnson 2015:21-4). See figure 1.3, a diagrammatical representation of the concurrent mixed methods design used in this study.

The quantitative component of this study is more dominant than the qualitative component. In this type of design, both quantitative and qualitative data are collected and analysed at the same time (Teddlie & Tashakkori 2006:20-21). Analysis of the quantitative and qualitative data is conducted separately. Then there is mixing of the data generated from the two methods, integrating the information gained from one method with that obtained from the other method. This integration of information is typically accomplished in the discussion and recommendation section of this study (Creswell 2009:2014:15). Each of the components of the design (quantitative and qualitative components) addresses specific segments of the main or primary research question of the study. Quantitative component was used to assess the treatment outcomes of patients with MDR-TB and its determinants for patients with MDR-TB

enrolled to the treatment with second-line anti-tuberculosis drugs. However, the quantitative data cannot provide detailed information about the context in which individuals provide information (e.g., the setting). As such, the qualitative component explored the contextual and naturalistic account of patients with MDR-TB and their caregivers regarding factors determining the MDR-TB treatment process, patients' perceived quality of care and patient satisfaction and adherence to the treatment of MDR-TB.

3.4.2. Rationale for choosing the concurrent mixed methods design in this study

The reason for employing a concurrent mixed methods design in this study, primarily emanated from the difficulty the researcher experienced in answering the research question investigated. The research question of this study required the use of a combination of qualitative and quantitative methods. The combined use of quantitative and qualitative methods helped to examine the different facets of the same phenomenon investigated, which in this case, relates to treatment outcomes of patients with MDR-TB (Edmonds & Kennedy 2017:181).

In other words, the quantitative and qualitative components of the research design enabled the researcher to investigate the research question from different perspectives. In this way, the design elucidates a detailed understanding of the research problem investigated. In other words, the qualitative and quantitative methods provided an enriched understanding of the factors determining the process and outcome of the treatment of patients with MDR-TB, including the patients' perceived quality of care and patient satisfaction with care given. Simply, the use of qualitative methods in this study helped to unfold the lived experience of patients with MDR-TB and their caregivers regarding the implementation of the MDR-TB programme. This indicates that the qualitative methods offered a contextualized understanding and explanation of the quantitative results of the MDR-TB programme (Caracelli 2006:86). Using either method alone (quantitative or qualitative) could not have fully addressed the research problem. Essentially, use of the mixed methods (quantitative and

qualitative methods) illuminated the associational processes and increased the interpretability of the results of this study.

The quantitative results were interpreted in conjunction with the qualitative results (meanings given by patients with MDR-TB and their caregivers). Thus, the combined use of quantitative and qualitative methods provided an increased understanding of the layers of meanings of the research problem investigated that could otherwise remain hidden (Hesse-Biber & Johnson 2015:88). The study investigated the treatment outcomes of patients with MDR-TB and the determinants (objectives 1 & 2 of the study).

The assessment of the treatment outcomes of patients with MDR-TB is the first objective of the study. The assessment of factors determining treatment outcomes of patients with MDR-TB is the second objective of the study. These two objectives were addressed using quantitative methods. The third objective of the study, which relates to patients' perceived quality of care and patients' satisfaction with care given on MDR-TB, was addressed using qualitative methods. In this study, the purpose of qualitative inquiry was to uncover meanings by eliciting memories of patients with MDR-TB who lived through the experience of the lengthy treatment for multi-drug resistant tuberculosis using second-line anti-tuberculosis drugs (Creswell 2009:114). The qualitative measure was used to supplement the quantitative result by uncovering meanings given by patients with MDR-TB and their caregivers (health care workers) regarding factors determining the MDR-TB treatment process and its outcome, the patients' level of satisfaction and their adherence to treatment (Stake 2010:31).

In summary, the quantitative and qualitative forms of evidence generated through employing the mixed methods design in this study, allowed stronger inferences to be made through complementarity than each method used alone (Gunasekare 2015:362).

3.4.3. The common advantages of the concurrent mixed methods design

Edmonds and Kennedy (2017:181-4) and Andrew and Halcom (2009:32) describe generic circumstances for using mixed methods in research studies. They note that mixed methods can be used:

1. to better understand a research problem by converging numeric trends from quantitative data and specific details from qualitative data.
2. when the research purpose and research questions require a combination of qualitative and quantitative methods.
3. to identify variables or constructs that may be measured subsequently through the use of existing instruments or the development of new ones;
4. to obtain statistical, quantitative data and results from a sample of a population and use them to identify individuals who may expand on the results through qualitative data and results;
5. to convey the needs of individuals or groups of individuals who are marginalized or under-represented.
6. when the research questions can be formulated to either provide testable results (quantitative) or to describe and characterize a phenomenon of interest (qualitative).
7. When there is insufficient information available in the literature and there is a need for exploratory research.

Some of the above reasons, particularly 1 and 2 are consistent with reasons for using a concurrent mixed methods design in this study. The use of this design was guided by a specific research paradigm, which is discussed below in detail.

3.5. The research paradigm- its assumptions

Researchers are required to commence research with assumptions that are aligned with research methodology, methods of data collection and analysis (Creswell, 2014). The researchers' assumptions that guide the conduct of a research study are sometimes referred to as paradigms (Morgan 2007:49; Wagner, Kawulich & Garner, 2012). A paradigm is a set of beliefs that guide researchers through the research process (Morgan 2014: 1046-7). It is a system of presuppositions within a research approach and it forms the framework within which solutions are sought for a research problem (Almekinders, Beukema &Tromp 2009:253). A paradigm is informed by philosophical assumptions about the nature of the truth or reality about a phenomenon (ontology), the researchers' position or stance in understanding the truth or reality of that phenomenon (epistemology), the values that researchers may attach or react to in the entire research process and the phenomenon under study (axiology) (Creswell 2014:26). There are commonly agreed worldviews. These are the positivism, post-positivism, constructivism, transformative and pragmatism worldviews (Saunders, Lewis & Thornhill 2007:102). These world views are the 'legitimated ways of knowing' (Bridges 2017:350). Of these worldviews, the pragmatism worldview is compatible with mixed methods research designs (Hall 2013:3-4). The ontology, axiology and epistemology that a research endeavour adopts are framed in terms of the choice made among the available research philosophies. As a study using a mixed methods design, this study adopts the position of the pragmatist philosophy or pragmatist paradigm.

3.5.1. The paradigmatic assumptions of pragmatic paradigm

The pragmatic paradigm assumes that reality is that which works and is practical (Ihuah & Eaton 2013:938). Pragmatic paradigm is considered as a bridge between qualitative and quantitative paradigms (Madondo 2015:7-10). According to the pragmatic paradigm, the most important determinant of the research philosophy adopted is the research question (Saunders, Lewis & Thornhill 2009:128).

Pragmatists focus on the value of knowledge and its ability to be integrated with a person's practical everyday understandings and choices. Philosophically, the pragmatists' position is against the position held by positivists who argue that reality is singular and objective (Neuman 2014:109). Pragmatism, as an alternative paradigm, accepts that philosophically, there are singular and multiple realities that are open to empirical inquiry. It orients itself towards solving practical problems in the real world. According to pragmatism, the measurable real world has different layers, some objective, some subjective and some are a combination of the two. Both objective as well as subjective inquiry attempt to produce knowledge that best represents reality. Thus, pragmatists are pluralists. They call for convergence between quantitative and qualitative methods. Moreover, pragmatists hold a view that research attempts should be useful or aim at its utility to solve real world problems (Feilzer 2010:8-9). As such, pragmatists argue that the most important determinant of the epistemology, ontology and axiology a researcher adopts is the research question under investigation. As it happens, one approach may be more appropriate than the other for answering a particular research question (Andrew & Halcomb 2009:21).

In the pragmatic philosophical view, the uses of both qualitative and quantitative methods to resolve a real-life world challenge are admired (Ihuah & Eaton 2013:937). Therefore, according to the pragmatist's view, it is perfectly possible to work with variations in one's epistemology, ontology and axiology. The use of mixed methods, both qualitative and quantitative, is not only possible but it is also highly appropriate to use within one single study (Saunders, Lewis & Thornhill 2009:109). Therefore, pragmatism is a philosophical partner for mixed methods design and is seen as

instrumental in achieving the research aims in the mixed methods design. According to pragmatism, the practical consequence of the research action is considered to be important and the research should be meaningful. Hence, clinical and applied research often benefit from the practical and instrumental approach of pragmatism (Johnson & Onwuegbuzie 2004:16). Pragmatism is intuitively appealing. It enables the researcher to study what is of practical value and uses the results in ways that can bring about positive consequences (Saunders, Lewis & Thornhill 2009:109).

Acknowledging this, a pragmatic paradigm is a guiding paradigm in social science research methods. It functions both as the basis for supporting work that combines qualitative and quantitative methods and as a way to redirect our attention to methodological rather than metaphysical concerns (Morgan 2007:48). This study adopts the pragmatic paradigm, as its assumptions are congruent with the study's methodology, and methods of data collection and analysis. The world reality investigated in this study has quantitative and qualitative layers. Therefore, some of the study questions need quantitative (objective) answers while others need qualitative (subjective) answers. The two set of answers serve a complementary function.

3.5.2. Ontological assumptions

Ontology is the researcher's view of the nature of reality or being (Porta & Keating 2008:353). It is an area of philosophy that deals with the nature of being, or what exists (Polit & Beck 2003:14). It asks what really is and what the fundamental categories of reality are (Neuman 2014:94). As researchers first start by asking philosophical questions about the reality they want to study, ontology is the starting point of all research (Sefotho 2015:30). Ontological assumptions give rise to epistemological assumptions, which in turn give rise to methodological considerations. It follows that methodological assumptions give rise to issues of instrumentation and data collection (Cohen, Manion & Morrison 2007:13).

Ontological assumptions of reality ask questions like whether reality is external to individuals or the product of individual consciousness (Polit & Beck 2004:14). The ontological assumptions of the qualitative research are that reality is constructed by

the researcher (constructivism). Whereas the ontological assumptions of the quantitative research view reality as objective and independent of the researcher (objectivism) (Ihuah & Eaton 2013:936)

Ontologically, pragmatists assume that reality is what works and is practical (Andrew & Halcomb 2009:186). It assumes that reality is external and multiple. The implication of ontological pragmatism for public health practice is that anything that works can be used to present the views of the researched (Madondo 2015:7). Pragmatic ontology assumes that the value of a research is not only based on whether it discovers the truth, but also on the demonstration that the results work with respect to the problem that is being studied (Mertens 2015:79). According to the pragmatic ontology, reality is both objective (exists independent of the actor) and subjective (that is, understood through the meanings that individuals attach to the social phenomena in which they live). Thus, a worldview that best enables researchers to answer the particular research question should be chosen (Saunders, Lewis & Thornhill 2009:109-10).

3.5.2.1. Ontological assumptions of this study

In this study, the research question under investigation has both objective (reality given out there in the world), and subjective (reality created by individual's own mind). Ontologically, the researcher's view is that social reality is one and it can be accessed using different methods, which work in conjunction with each other (Johnson, Onwuegbuzie & Turner 2007:120). In this study, the researcher's view is that the research question under investigation has different layers. These layers are the result of both the physical natural world as driven by the real natural causes (objective) and the influence of human experience and interpretation, which is multiple, subjective and mentally constructed by individuals (Östlund, Kidd, Wengström & Rowa-Dewar 2011;370). As such, both quantitative (objective) and qualitative (subjective) data were collected to get full insight into the factors that determine treatment outcomes of patients treated for MDR-TB, including patients' perceived quality of care and patients' satisfaction with care given for MDR-TB. Quantitative data on patients' socio-demographic and clinical characteristics were collected using a structured

questionnaire. Qualitative (narrative) data were collected using a semi-structured interview guide.

3.5.3. The axiological assumptions

Axiology relates to people's values, moral principles and how these may influence behaviours and the conduct of a research (Harrington 2015:16). In practice, our values are the guiding reasons for all our actions. It is a way to consider values along with the issues of research ontology, epistemology, and methodology (Creamer 2018:43-48; Morgan 2007:58).

The pragmatic axiological, assumption argues that knowledge is gained in pursuit of its desired ends (Saunders, Lewis & Thornhill 2009:119). Therefore, researchers are concerned with issues that are good for research (Madondo 2015:7). Pragmatic axiology assumes that values play a vital role in interpreting research results using both subjective and objective reasoning (Ihuah & Eaton 2013:937). The axiological assumption of pragmatism, aligns with the utilitarian theory of ethics. It holds that the value of something is a function of its consequences. It describes the ethical stance of pragmatism as gaining knowledge in pursuit of its desired ends. This means that rather than doing a research for the sake of research interest, pragmatists see the value of the research as how it is used and the results of that use (Mertens 2015:79). Axiologically, pragmatism is concerned with any value that works and discusses values that work (Madondo 2015:7-9). As such, axiology refers to the values that researchers may attach to the entire research process (Marcum 2015:215). It is the role that the researcher's own value may play in the research process. This is of great importance if the researcher wishes that his or her research results are credible. In a nutshell, axiology is about the researcher's own personal values in relation to the topic studied. Thus, the axiological assumption of the pragmatic paradigm is that values play a large role in pursuing a research and in interpreting the results of a research (Saunders, Lewis & Thornhill 2009:116-19).

3.5.3.1. Axiological assumptions of this study

When registered for a doctoral programme at the University of South Africa, the researcher is bound by the ethical principles of beneficence regarding the topic to be researched. That is, what benefits would patients with MDR-TB gain from being researched (Mertens 2015:77). This principle was guided by the researcher's (inquirer's) own personal experience with the programme of the management of MDR-TB in the Oromia Region of Ethiopia. This experience includes that there is lack of evidence on the factors determining the management of drug-resistant tuberculosis in the Oromia Region of Ethiopia. The lack of evidence has motivated the investigator to play a catalytic role in generating evidence that can trigger evidence based decision making for the management of MDR-TB. This reason guided the decisions made by the researcher at all levels of the research process. The researcher had the experience that individuals affected by MDR-TB face social and economic problems. The experience of and the combination of the disease and economic constraint is a difficult place to be in for patients with MDR-TB. For patients treated for MDR-TB, this is an unrecognized problem. The focus is on the biomedical response to the problem of MDR-TB following the international approach to the management of drug-resistant tuberculosis. This results in complaints and sometimes interruption of treatment by patients with MDR-TB. This has been a striking experience for the researcher.

As per the researcher's own experience, no one knows whether patients with MDR-TB are comfortable with the current approach to the management of MDR-TB. On the other hand, the management of patients with drug-resistant tuberculosis is a recent undertaking in the Oromia Region of Ethiopia. Most of the treatment outcomes of patients with MDR-TB published so far in Ethiopia, are based on those patients treated at the best centres that are funded by non-governmental organizations in collaboration with the Ministry of Health of Ethiopia (Meressa et al 2015:1181).

In Ethiopia, the MDR-TB programme is shifted from the primarily hospitalized in-patient care model to the ambulatory model of care. It was believed that, as the ambulatory model of care is community based, it allows the decentralization of the services given

for MDR-TB and thus improves service accessibility to the community (Federal Ministry of Health of Ethiopia 2014:10). However, there is no evidence regarding the treatment outcomes of patients with MDR-TB treated in the predominantly outpatient model of care. Evidence is also lacking on the perception and experience of patients with MDR-TB regarding the current approach to the management of drug-resistant tuberculosis. The researcher believes that the lack of evidence in these areas has curtailed evidence based decisions to institute appropriate intervention measures. As such, the real-life experience of the researcher and lack of evidence at programme level has encouraged the researcher to be of service to the community. For the researcher, that commitment became a reality by uncovering the challenges and factors that affect the programmatic management of drug-resistant tuberculosis in the Oromia Region of Ethiopia. As such, the investigator hopes that by facilitating evidence informed decision making, the result of this study will advance the benefits of patients infected and affected by drug-resistant tuberculosis in the Oromia Region of Ethiopia (Greene 2006:93).

3.5.4. The epistemological assumptions

Epistemology is about "how we know what we know" (Andrew & Halcomb 2009:121). It is about determining the relationship between the knower (researcher) and what is known (Greene 2006:93). Epistemology is concerned with the nature and forms of knowledge and how it can be acquired and communicated to others (Cohen, Manion & Morrison 2007:7). There is a relationship between ontology and epistemology. Ontology is about the nature of the truth out there, and epistemology connects to ontology by asking the question about the possibility of knowledge generation regarding the truth in the form of 'objective' or 'subjective' knowledge (Morgan 2007:57). Epistemologically, pragmatism asks the question of the type of relationship between the researcher and the researched. It assumes that there may be distance or no distance between the researcher and the researched (Madondo 2015:7-9). For a researcher engaged in a particular study, it is more appropriate to think of the philosophy of 'a distance' and 'no distance' when depicting the relationship between the researcher and the researched as existing on a continuum rather than occupying opposite positions of the continuum. At some points of the continuum, the knower and

the known must be interactive, while at other points, one may more easily stand apart from what one is studying (Saunders, Lewis & Thornhill 2009:109).

Thus, the epistemological assumptions of pragmatism are that either objective or subjective meanings or both can provide facts to a research question. It focuses on the practical application to issues by merging views to help interpret data (Ihuah & Eaton 2013:938). Therefore, in pragmatic epistemology, the researcher is free to develop whatever type of relationships with participants that are appropriate for the matter under investigation. The nature of the relationship between the researcher and the participants is judged in terms of its ability to get the results of the study to be used by the intended stakeholders (Mertens 2015:79). Thus, either or both observable phenomena and subjective meanings can provide acceptable knowledge dependent upon the research question. Pragmatic epistemology focuses on practically applied research. It assumes that integrating different perspectives help to better interpret the research data (Saunders, Lewis & Thornhill 2009:119).

3.5.4.1. The epistemological assumptions of this study

In this study, the reality under investigation has both subjective and objective components. (Johnson, Onwuegbuzie & Turner 2007:120). In relation to the objective component, the study made careful observations and acquired empirical evidence on the factors that might determine the treatment outcomes of patients with MDR-TB and its determinants. In this case, there was minimum space for subjectivity and the researcher was independent of the phenomenon investigated. As such, the plausible relationship between the independent and the dependent variables of interest stated in the hypothesis of the study was tested deductively. On the other hand, factors that might determine patients' perceived quality of care and patient satisfaction with care given for MDR-TB were generated through the detailed description of the viewpoints, experiences and interpretations of patients with MDR-TB and their caregivers. Here, the researcher was always part of the discovery process. The researcher inductively observed, interpreted, and reflected on what the patients and caregivers said about the programmatic management of drug-resistant tuberculosis. The researcher also

simultaneously reflected on his own personal experiences and interpretations regarding the same.

In this study, the quantitative and qualitative data were used to answer related aspects of the same research question. To respond to specific objectives (1 & 2) of the study, the researcher collected quantitative data on treatment outcomes of patients with MDR-TB and its determinants. Epistemologically, this quantitative data generated objective rather than subjective knowledge. Thus, quantitative (objective data) were collected using a structured questionnaire. Quantitative data were collected on the patients' socio-demographic and clinical characteristics. More quantitative data were collected on patients' adverse drug-reactions from second-line anti-tuberculosis drugs. For the specific objective 3 of this research study, the researcher collected qualitative data on patients' level of perceived quality of care and patients' satisfaction with care given for MDR-TB. Epistemologically, these data generated subjective than objective knowledge of the subject studied (Morgan 2007:57). This manner of generating narrative data enabled the researcher to come closer to the researched (participants of the study). Narrative data were collected using interviews with the help of an interview guide.

3.5.5. Methodological assumptions

Epistemologically, pragmatism assumes that an investigator is free to develop a relationship with a participant that is appropriate for the matter under investigation. This relationship is judged in terms of its ability to enable the researcher to achieve the aims and objectives desired in a study (Mertens 2015:79-80). In this way, the underlying methodological assumption of pragmatism is that the research method should match the purpose of the research (Mertens 2015:79). It assumes that any methodology (quantitative or qualitative) can be used provided it brings about valid and reliable results. Thus, a research can be conducted deductively or inductively or both through the use of both quantitative and qualitative data collection methods (Madondo 2015:7-9). In other words, pragmatic methodology advocates for choosing a combination or mixture of methods and procedures that works best for answering the research question under investigation. It however stresses that the research methods used must

match the specific research questions and the purpose of the study (Creswell 2009:28-29). This suggests that one of the primary aims of methodology pragmatism is to interrogate a particular question, theory, or phenomenon with the most appropriate research methods (Feilzer 2010:13). Methodology pragmatism stresses on the use of a pluralistic approach to study a research problem. In this way, pragmatism is a philosophical basis for mixed methods research whereby the inquirers draw liberally from both quantitative and qualitative assumptions (Creswell 2009:10).

3.5.5.1. Methodological assumptions of this study

The study used a pragmatic methodological approach. This approach enabled the best use of the study results to enhance the management of patients with MDR-TB.

The study combined both deductive and inductive approaches to test the different segments of the research hypotheses. The researcher used the deductive approach to test hypotheses regarding the treatment outcomes of patients with MDR-TB and its determinants. It used empirical observations on purposively selected patients with MDR-TB to generate empirical evidence on treatment outcomes of patients with MDR-TB and its determinants. Hypotheses were set regarding the plausible relationship between the independent and dependent variables included in the study. Variables were operationalized, based on international standards and the available literature. Data were collected by administering a structured questionnaire to purposively selected patients with MDR-TB.

The study also used the views, the perspectives and the interpretations of patients with MDR-TB to explore factors determining patients' perceived quality of care and patient satisfaction with care given for MDR-TB. The inductive (subjective and contextual) approach was used to understand the meanings that patients with MDR-TB attributed to their behaviour and to the external world surrounding the treatment given for MDR-TB (Porta & Keating 2008:26). The experience and practices of caregivers for MDR-TB were also used to explore and understand the functionality of the programmatic management of MDR-TB at the study sites. Qualitative data were collected by interviewing patients with MDR-TB and their caregivers. The feelings, and the experiences of the patients with MDR-TB, patients' perceived quality of care and their

satisfaction included how patients coped with the problem of MDR-TB and was explored inductively. In the same, the experience and practice of caregivers for MDR-TB were explored. Specifically, the study:

- tested quantitative hypothesis by measuring the relationship between the quantitative independent and the dependent variables included in the study. It tested the relationship between MDR-TB treatment outcome and the socio-demographic and clinical characteristics of patients with MDR-TB. These hypotheses were tested deductively by collecting quantitative data through the administration of a structured questionnaire. Data was collected from purposively selected patients with MDR-TB enrolled to treatment for MDR-TB at the two selected hospitals.
  - For the deductive approach, research hypotheses were formulated. The hypotheses were generated from the review of the relevant literature on the factors determining the treatment outcomes of patients with MDR-TB. Moreover, the researcher's previous experience on the management of patients with MDR-TB and the desire to contribute to the management of patients with MDR-TB in Ethiopia, were sources for the hypotheses generated for testing deductively (Lancaster 2005:23-5).

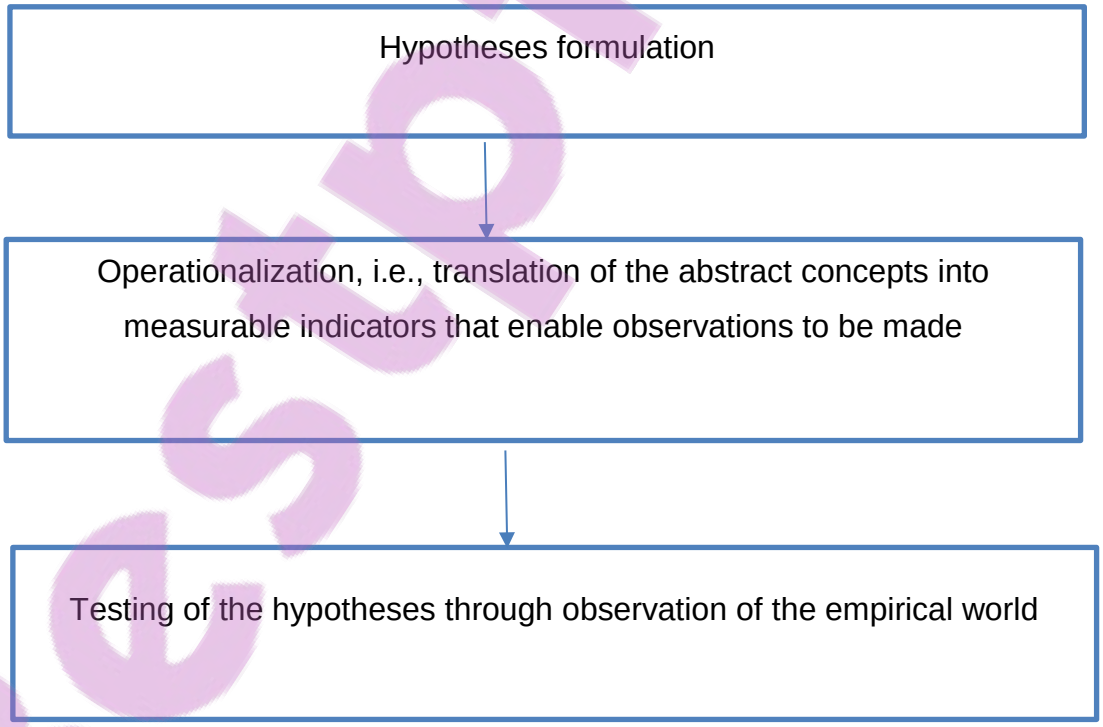


Figure 3. 3. The process of deductively testing the quantitative objectives of the study

- For the qualitative research questions, the study used the interview approach to understand the meanings and interpretations that patients with MDR-TB and their caregivers attach to the social and environmental factors surrounding the care given for MDR-TB (Parvaiz, Mufti & Wahab 2016:72). As such, it explores and describes the relationship among patients' social, financial situations, available patient support schemes, the condition of the service set-ups and level of patients' perceived quality of care and patients' satisfaction with care given for MDR-TB. The second part of the research question was tested inductively by collecting qualitative data generated through interviewing patients with MDR-TB and their caregivers.

3.6. Research methods

3.6.1. Introduction

Research method refers to the structure of the sequences of actions followed in a research process. It covers the choices made regarding what is to be done and the order in which it is done (Singh 2006:99). In this research endeavour, there were certain practical phases. Polit and Beck (2003:47-58) outlines five basic phases in pursuing a given research process. These phases include: 1) the conceptual phase 2) the design phase 3) the empirical phase 4) the analytical phase and 5) the dissemination phase. These phases were followed in this study and each one is briefly described as follows:

3.6.1.1. The conceptual phase

The selection of the research topic of this study emanated from the researcher's passionate interest to investigate factors that might influence MDR-TB. Such interest was rooted in the researcher's professional experience of the clinical and programmatic challenges associated with the management of MDR-TB. Moreover, the researcher learnt that there was no evidence on the determinants of treatment outcomes of patients with MDR-TB. There was also no evidence regarding patients' perceived

quality of treatment for MDR-TB. These observations were the root of the researcher's inspiration to conduct a study on MDR-TB. As a result, the research question of this study was informed by the researcher's real-life experience on MDR-TB, which is a priority subject in the Oromia Region of Ethiopia.

Then a literature review was conducted to learn about the status of the contemporary knowledge of the global approach to the management of MDR-TB. The rationale was to identify gaps in knowledge in relation to the management of MDR-TB. The literature revealed that the research question developed and its related research problems were complex, and they needed quantitative and qualitative approaches to fully investigate them. The literature also led to the identification of the conceptual framework to guide the study. The research hypotheses of the study were formulated to investigate the associations between the independent and dependent variables of interest.

3.6.1.2. The design phase

This study has a main research question and a number of sub-research questions. While most of the sub-questions could only be investigated using qualitative methods, some could be investigated using quantitative methods. Given this, a decision was made regarding the type of research design that could enable the researcher to fully investigate the research questions of the study. A design that was considered appropriate for achieving this was concurrent mixed methods with quantitative dominance.

3.6.1.3. The empirical phase

At the empirical phase of this study, decisions were made regarding the procedures of data collection, the study instrument to be used and procedures of its administration. It was made clear that the quantitative component of study used a structured questionnaire to collect patient's clinical data. The questionnaire was developed using the extant literature, and opinions of the supervisor and experts in MDR-TB. The experts conducted a serial review of the questionnaire before it was subjected to a preliminary investigation.

The questionnaire was tested in the field and was further refined based on the outcomes before its use on the main study participants. Trained data collectors administered the final questionnaire. The questionnaires administered to participants were given unique codes to ensure anonymity. The qualitative data were collected using in-depth interviews with patients with MDR-TB and their clinical caregivers. The in-depth interviews were conducted by the principal investigator but he was assisted by a trained data collector assistant (note taker).

3.6.1.4. The analytical phase

At this phase, the decisions regarding the organization of the data, data analysis, interpretation and writing of the results of the study, were taken for both the quantitative and qualitative data gathered in this study. Using the statistical package for social sciences (SPSS) version 23, a template was developed for the quantitative data entry and analysis. The qualitative data and qualitative data were analysed concurrently but separately. On completion of the analysis, both quantitative and qualitative data sets were integrated at two levels: result section, and discussion section of the study.

3.6.1.5. The dissemination phase

This phase of the research process is concerned with the communication of the end results of a research to an appropriate research community for translation and use by the intended beneficiaries. The researcher of this study planned to disseminate the full reports of the study to the global research community through the University of South Africa's (UNISA) electronic repository. Moreover, the result of this study will be disseminated to individual health professionals globally by means of journals and other electronic media.

3.7 The study population

3.7.1. The source population

The source population is the universe of interest that consists of all the people or other entities that researchers would like to study if they had infinite resources (Crano, Brewer & Lac 2015:220). In other words, a source population is the entire population of people or things to which the results of a study are meant to apply (Field 2009:34). The population may be persons, things, or measurements for which we have interest at a particular point in time. Our sphere of interest determines a population. Population can be finite (consists of fixed number of values) or infinite (consists of an endless succession of values) (Khanal 2016:7). Researchers would like to generalize their results about the population of interest (Boslaugh 2013:54-5).

3.7.2. The source population for this study

The source population for this study was all patients with MDR-TB, those enrolled to treatment with second-line anti-tuberculosis drugs at all treatment initiating centres in the Oromia Region of Ethiopia.

3.7.3. Study population

3.7.3.1. Definition of the study population

Usually we can never have access to the entire source population for inclusion in a study (Field 2009:34). Thus, the information required to find answers to the study's questions is obtained from the study population. The study population is defined as that of the aggregate of elements to which the researcher can gain access and from which the research sample is actually selected (Babbie 2014:207). The results of a study apply to that group of the study population. As one narrows the research problem, similarly it is crucial to decide very specifically and clearly, who constitutes the study population in order to select the appropriate participants (Kumar 2011:43). The study population provides a boundary between that segment of the source population that is included in the study and that segment that is not included in the study (Boslaugh 2013:15).

3.7.3.2. The study population for this study

It was not practical to access all patients with MDR-TB and all caregivers for MDR-TB practicing in the Oromia Region of Ethiopia. As such, patients enrolled to MDR-TB treatment and their caregivers at two referral hospitals in the Oromia Region of Ethiopia were accessible and constitute the study population. Thus, study population for this study was all patients with laboratory confirmed MDR-TB enrolled to the treatment for MDR-TB and the caregivers for MDR-TB at the two referral hospitals in the Oromia Region of Ethiopia.

3.7.3.3. Eligibility criteria

3.7.3.3.1. Inclusion and exclusion criteria

The goal of describing eligibility criteria is to determine who will be eligible to participate in a particular study. In any study endeavour, eligibility criteria is used to recruit participants to make sure that the ultimate study results address the pre-determined research questions. Describing eligibility criteria typically involves describing both inclusion and exclusion criteria. Inclusion and exclusion criteria have the goal of identifying a population in which it is feasible, ethical and relevant to a particular research endeavour. In essence, study participants that can sufficiently enable assessment of the risk factors, the quality or the outcomes of interest are selected using inclusion and exclusion criteria. (Hulley, Cummings, Browner, Grady & Newman 2013:143-4):

3.7.3.3.2. Inclusion criteria

- All laboratory confirmed patients with MDR-TB who had been on treatment for MDR-TB for a period of six months and above at the time of data collection were included in f the study.
- All patients with MDR-TB aged 18 years and above at the time of data collection were included in the qualitative component of the study
- Caregivers who were actively giving care to patients with MDR-TB were included in the study.

3.7.3.3.3. Exclusion criteria

- All laboratory confirmed patients with MDR-TB who had been on MDR-TB treatment for less than six months at the time of data collection were excluded from participating in the study
- Patients with laboratory confirmed MDR-TB aged below 18 years at the time of data collection were excluded from participating in the study.

3.7.3.4. Sampling methods and the sample size: Quantitative component

In any research endeavour, data are gathered with the aim that it contributes to a better understanding of the research question under investigation. Then it becomes imperious that selecting the manner of obtaining the necessary data and from whom to acquire the data should be done with sound judgement. This is because no amount of analysis can make up for improperly collected data. The quality of a research can be determined not only by the appropriateness of its methodology and instrumentation, but also by the sampling strategy used. Collecting data from the whole population might be impossible and expensive. Hence, a sample of a population of interest is often used to collect data (Boslaugh 2013: 83-4).

In this study, certain procedures were followed and decisions were made to select samples for the study. By the time of the data collection, a total of 182 patients with MDR-TB were registered between 26 December, 2012 and 17 September, 2016 at Adama and Nekemte referral hospitals. From the total of 182 registered patients with MDR-TB, 46 (25%) did not meet the inclusion criteria so that they were excluded from the study. The remaining 136 (75%) of the patients with MDR-TB fulfilled the set inclusion criteria of the quantitative component of the study, that is, the need to be on treatment for MDR-TB for a period of six months or above at the time of data collection. From total patients who met the inclusion criteria for the quantitative component of the study, twenty three (23) participants those aged 18 years and above by the time of data collection were sampled for the in-depth interviews with patients.

As such the total sample size for the quantitative component of this study was 136 patients with MDR-TB. The rationale behind including all the participants who meet the inclusion criteria, was to make sure that a sufficient number of the required sample size

was included in the study so that the resulting statistics could help draw conclusions and inferences could be made based on the study sample. Therefore, the 136 sample size was used to achieve an acceptable level of power to test the null hypothesis of no relationship between the treatment outcomes of patients with MDR-TB and their clinical and sociodemographic characteristics (Figure 3.5, below depicts the diagrammatic representation of the sampling procedure used for the quantitative component of the study).

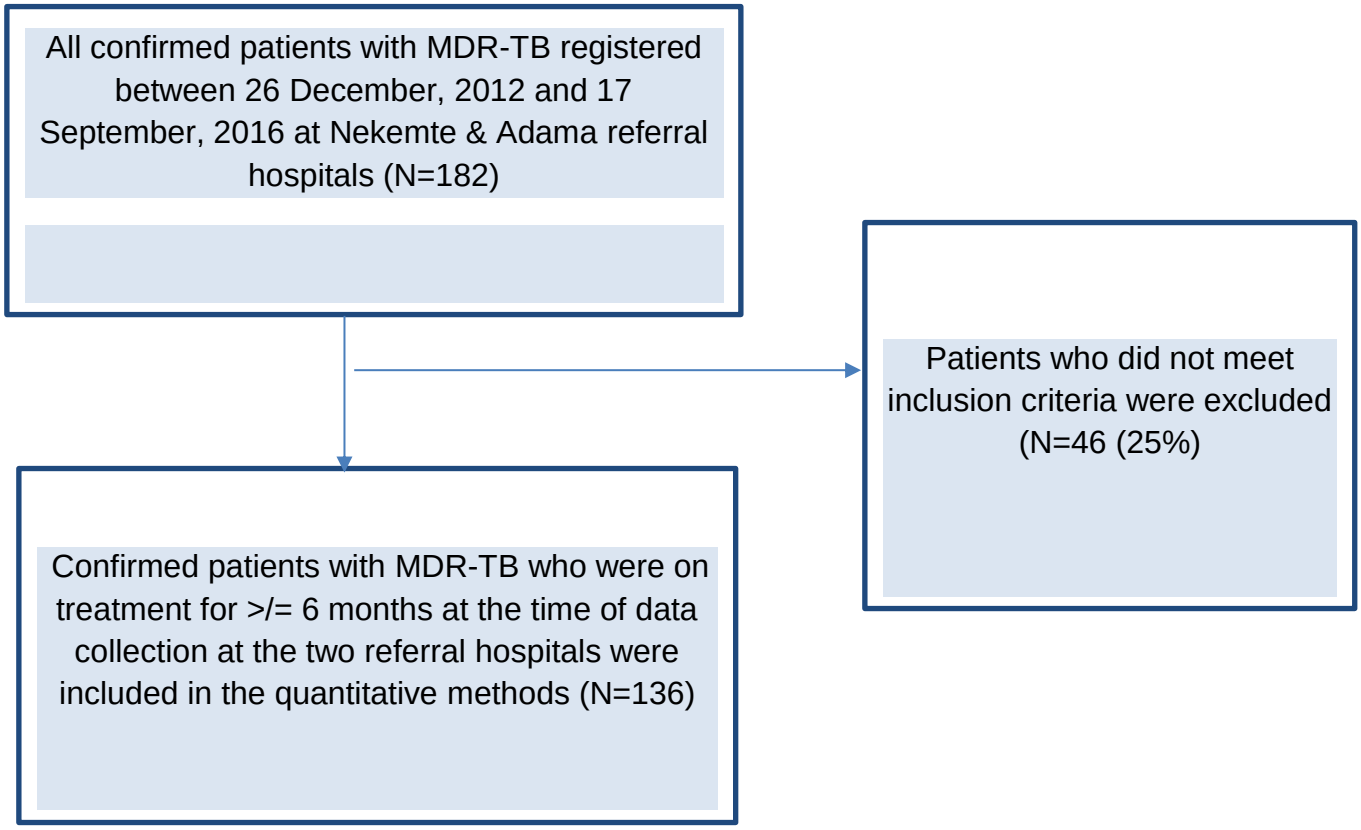


Figure 3. 4. Diagrammatic representation of the sampling procedure used for the quantitative component of the study.

In this study, statistical power was calculated for the sample included in the study. The power of a statistical test is the probability of rejecting null hypotheses that are rejectable (Boslaugh 2013:375). As such, statistical power was calculated to make sure that the sample taken was sufficiently large to test the null hypothesis of the study. In this study, the hypothesis of no difference in the treatment outcomes between patients

with different clinical characteristics was a major outcome variable. The major variable among the clinical characteristics of patients with MDR-TB was the presence of co-morbidity with MDR-TB.

There were two groups with respect to this. These groups were patients with co-morbidity (p1) and patients without co-morbidity (p2) with MDR-TB at the baseline. From the literature P1 & P2 for this study were, P1=0.81 and p2= 0.70 (Meressa et al 2015:1183). Then power calculation formula for one sample proportion was used to calculate power for the total sample size used for the quantitative component of this study. Accordingly the calculated power for the sample size included in the quantitative component of the study was 0.87. It was for this reason that the records of all the 136 participants who meet the inclusion criteria at the Adama and Nekemte Referral hospitals were retrieved and included in the study.

3.7.3.5. Sampling method and sample size: Qualitative component

Sampling for the qualitative component of this study focused on patients with laboratory confirmed MDR-TB and healthcare professionals who were caregivers for patients with MDR-TB for the following reasons. Patients with MDR-TB have the unique socio-demographic and clinical characteristics that the study attempts to investigate. Moreover, these patients have the experience of MDR-TB and the lengthy treatment associated with the disease. The sampling of this component of the study also focused on caregivers with the experience of treating patients with MDR-TB. This professional group has the experience in the clinical, programmatic, socio-economic and psychological aspects related to the management of patients with MDR-TB.

Patients with MDR-TB and their caregivers were selected using purposeful sampling methods in order to elicit their experiences of this condition. Patients with MDR-TB were approached to participate in the study during their monthly visits to the Adama and Nekemte referral hospitals for their scheduled follow up services at the two hospitals. During the data collection period which was from the 10th of November 2016

to the 7th of February 2017, all the 136 eligible patients with MDR-TB had at least a one-time visit to the hospitals for their scheduled monthly follow up services. Some of these patients were treated as inpatients. From the total number of patients who attended the scheduled follow up services at the two hospitals, 22 information rich patients with MDR-TB who were aged 18 years and above were purposively sampled in collaboration with the attending health nurses and physicians. Some of the 22 patients with MDR-TB included inpatients at the treatment centres of the two hospitals.

From the total of 23 patients sampled 2 patients did not volunteer to participate while the rest (21 patients) volunteered for participation. However, successful in-depth interviews were conducted with eighteen (18) patients with MDR-TB. The total of 18 patients who participated in the semi-structured interviews was determined by category saturation. This was the point at which the interviews did not reveal new data relevant to the aims and objectives of the study.

In relation to caregivers, a total of 11 (physicians and nurses) were purposively sampled and participated in the semi-structured interviews. The 3 of the 11 caregivers were physicians while 8 of them were nurses. The total number of caregivers sampled and who participated in the semi-structured interviews was also determined by category saturation. The 11 caregivers were all active caregivers for patients with MDR-TB, and they were accessible at the time of data collection and participated in the in-depth interviews with caregivers.

3.8. Data collection

3.8.1. Data collection tools

The researcher developed the data collection tools for both components of this study (quantitative and qualitative). The main focus in the development of the study tools was to make sure that the responses obtained from participants were valid and reliable. (Crano et al 2015:219-20). Hence, the development process of the tools was guided by the study's specific research objectives and followed the standard scholarly recommendations.

3.8.1.1. Data collection tool development: quantitative component

The data of this component of the study was collected using a structured questionnaire. The researcher followed key steps to develop the questionnaire.

- The researcher reviewed contemporary literature relevant to the study subject area, MDR-TB. Variables relevant to the subject area were extracted from the literature reviewed.
- The extracted variables were then examined in line with the aims and objectives of the study.
- The variables extracted were discussed with the supervisor of this study and experts in the study area, MDR-TB.
- The researcher then developed the first draft of the questionnaire. This was reviewed three times by the researcher before seeking expert opinion.
- Experts in the field and supervisor reviewed the draft questionnaire.
- Comments from experts and supervisor were incorporated to make sure that:
  - ✓ The questionnaire is sensitive to measure what it meant to measure,
  - ✓ The questionnaire is understood in the same way if used by different researchers.
- Comments from experts and supervisor were incorporated in the questionnaire. In other words, the questionnaire was revised in line with comments offered by the supervisor and experts.

3.8.1.2. Components of the quantitative data collection tool

The quantitative tool was made, as comprehensive as needed to capture all the necessary data required to fully answer the problem under investigation. As such, it had sections that captured data on the different segments of the problem under investigation. These included (see annexure 2, part I):

- Background information on the socio-demographic and socio-economic characteristics of the study participants.
- Participants' background information on the basic tuberculosis related data, including the diagnostic modalities used in the diagnosis of patients with presumptive tuberculosis
- Current MDR-TB related information of the participants
- Clinical characteristics of the patients with MDR-TB including status of baseline co-morbidity with MDR-TB, the presence of malnutrition with the MDR-TB disease
- The status of drug susceptibility test services for patients with MDR-TB
- The standard clinical management of patients with MDR-TB
- The status of patient treatment support under daily observable treatment
- The status of MDR-TB and HIV co-management for patients infected by both diseases
- Collaboration between treatment initiating hospitals and the treatment initiating centres in providing a continuum of care for patients with MDR-TB
- The status of occurrence of adverse drug reactions and its management
- The programme efforts in MDR-TB infection prevention and control at the health facility and community levels.
- Availability status of clinical, radiological and laboratory follow up services for patients on treatment for MDR-TB
- The inspection of premises of the MDR-TB treatment centres of the two referral hospitals
- Interim and final treatment outcomes of patients with MDR-TB

3.8.1.3. Data collection tool development: qualitative component

The data collection tool of this component of the study was a semi-structured interview guide. The interview guide was developed taking into consideration the aims and objectives of the study. The development of the interview guide was also shaped or underpinned by the literature reviewed. Simply, concepts relevant to the study area from the literature reviewed were used in developing the interview guide. It consists of a number of open-ended questions, probes and prompts (see annexure 2, part III & IV).

3.8.1.4. Components of the qualitative data collection tools

The qualitative tool used for the in-depth interviews with patients encompassed the patients' socio-demographic status and the patients' level of awareness of MDR-TB. It contained questions on patients' perception on the socio-economic impact of becoming a patient with MDR-TB and the status of the socio-economic support provided for patients through the programme of MDR-TB. This part also contained items on the level of the accessibility to the care given for MDR-TB both at the hospital and the community level. It also contained question items to explore the level of the responsiveness of the caregivers in providing a care that is prompt and consistently accessible on demand. To that end, the tool contained patients' perception on the quality of the care given for MDR-TB and level of their satisfaction with the overall care and services that they obtained on MDR-TB.

The qualitative tool used for the in-depth interviews with caregivers contained question items that were used to explore caregivers' professional background and their perception and practices regarding the status of the functionality of the MDR-TB programme. This part also contained question items on the practices of caregivers in providing the continuum of the clinical and programmatic care needed by patients with MDR-TB. It also contained question items that explored the level of the system's support to improve the functionality of the MDR-TB programme including the availability of integrated care for patients infected with other diseases on top of the MDR-TB like the HIV/AIDS and diabetes mellitus (see annexure 2, part III & IV).

3.8.1.5. Piloting the data collection tools

The questionnaire was piloted on a sample of patients with MDR-TB and caregivers for MDR-TB who practice in another hospital similar to the two hospitals selected for the main study. The data obtained from the pilot was entered into SPSS version 23. The outcome of the analysis resulted in the revision and refinement of the questionnaire. The revised questionnaire was used for quantitative data collection in the quantitative component of the study (see annexure 2, part I).

The interview guides were also piloted on a sample of patients and caregivers for MDR-TB. This was done to ensure that the participants understood the questions included in the guide. Comments from participants who took part in the pilot led to the revision of the interview guide. The revised interview guides were used as data collection tools in the qualitative component of the study (see annexure 2, part III & IV).

3.8.2. Data collectors

Two data collectors who were healthcare professionals, collected the data for the quantitative component of the study. The data collectors were offered a two-day training on data collection, which included discussions on the structure, content of the questionnaire of the study, and its application. Following training, the data collectors actively participated in the pilot of the questionnaire on a sample of patients with MDR-TB who were receiving treatment in other hospitals similar to those which participated in the main study. The rationale for this was to enhance their familiarity with the questionnaire and ensure consistency in its use.

The data of the qualitative component of the study were collected by the principal investigator. The principal investigator did not require any training on collecting the qualitative data, as he has many years of experience of data collection using individual and focus group interviews. The data of this component of the study was collected from patients with MDR-TB and their caregivers using a semi-structured interview schedule.

3.8.3. Type of data collected: quantitative component.

Baseline data were collected on participants' socio-demographics data, including age, sex and place of residence and education level. The data collectors, with the help of a structured questionnaire, collected the quantitative data from patients' medical records (that is patient clinical charts, the unit MDR-TB register and patient treatment cards. Data were also collected on patients' clinical characteristics. Patients' clinical data included the chemotherapeutic regimens used to treat patients, co-morbidities with MDR-TB at baseline and baseline sputum smear status. Data were also collected on MDR-TB diagnosis modalities, the patients' drug-sensitivity test patterns and the patients' previous tuberculosis treatment history. Clinical data collected included the patients' HIV sero-status (T-lymphocyte cell bearing (CD4) count) use of cotrimosaxole preventive therapy and anti-retroviral therapy by patients with MDR-TB as well as the patients' MDR-TB and HIV co-infection.

The clinical data collected also included adverse effects from second-line anti-tuberculosis drugs. The patients' adherence to the daily observable treatment, laboratory and radiography follow up services, and treatment results of patients with MDR-TB.

3.8.4. Type of data collected: qualitative component

Data were collected on the lived experience of patients with MDR-TB using a semi-structured interview guide. The data collected focused on the patients' level of awareness of the disease and its treatment, the patients' level of engagement with treatment decision making, patients' perception and experience on the social and economic impact of becoming a patient with MDR-TB, patient support schemes, patients' perceived quality and satisfaction with the care provided. In addition, data were also collected from caregivers of patients with MDR-TB on their experiences and practices regarding the clinical and programmatic management of MDR-TB. Notes were taken during the individual interviews by a trained note-taker. Each of the individual interviews was audio-recorded as back up. Notes were taken by a note-taker during the process of interviews with patients with MDR-TB and their caregivers.

3.9. Data analysis

3.9.1. Data analysis: quantitative component

The quality of data analysis is dependent upon the quality of data. Thus, the study data of this component of the study were managed before analysis. Data management entails working directly with data. It involves cleaning, organizing data for analysis (Boslaugh 2013:411-2). Data analysis on the other hand refers to the computation of certain measures and searching for patterns of relationships among data groups.

Each completed questionnaire was checked for completeness, and was coded before data entry. The Statistical Package for Social Science (SPSS) version 23 was used for data entry, data cleaning, data management and analysis. The data were entered into SPSS, cleaned, and the researcher familiarized himself with the study variables (like numeric and string) before data analysis. The researcher made sure that each variable had an appropriate label that linked it to the value in the questionnaire.

On completion of data cleaning, descriptive statistical analyses for each variable of interest were computed taking into account the objectives of the study. Examples of the descriptive statistics computed include frequencies, measures of central tendencies and dispersion. Frequencies were the first descriptive statistics computed. In instances where missing values for variables were observed, this was addressed by reverting to the raw data on the questionnaire and re-entering the correct value of the variable.

Subsequently, measures of association between the variables of interest were computed. The Chi-square, univariate and multi-variate logistic regression analyses were employed to identify the independent predictors of the outcome of interest, that is, factors associated with the level of MDR-TB treatment outcomes among patients treated for MDR-TB. Confidence intervals and p-values were used to test the significance of the observed sample parameters in exploring determinants of MDR-TB treatment outcomes (Singh 2006:227).

3.9.2. Data Analysis: Qualitative component

For the qualitative component of this study, coding and analyses was done manually. Manual analysis was chosen not to miss nuances or latent meanings. The researchers are instrumental to the quality of the research outcomes by the questions they ask, how they code and how they explore the underlying meanings (Leavy 2017:147-8). Moreover, manual manipulation of the data helps the researcher to focus on the data so that manual analyses gives the researcher more control over the data and ownership of the work done (Saldaña 2013:26).

The central issue in the qualitative data analysis is making sure that the research participants' subjective meanings about the social reality under investigation are appropriately conveyed in the final report. In qualitative data analysis, meanings are conveyed in terms of themes and their related sub-divisions or sub-themes. A theme is defined as an attribute, a descriptor or a concept that organizes repeating ideas or codes of similar points of reference regarding the subject of inquiry. A theme unifies ideas at the interpretive level and it helps answer the study questions. Sub-themes help to obtain a comprehensive view of the data and uncover patterns in the participants' accounts (Vaismoradi, Jones, Turunen & Snelgrove 2016:101).

In this study, for every audio-taped interviews, its verbatim transcription was started immediately after completion of the interviews and completed within 48 hours. This helped to make sure that important ideas were not missed as a result of delays as ideas could be forgotten with time. During the whole process of the interviews, the preliminary scanning of emerging themes was serially analysed to identify points of saturation in each category as ideas were emerging out of the study participants.

The qualitative data analyses were made inductively from the specifics of the qualitative data and the coded data into the general themes, patterns and their interpretations. As such, the qualitative data was analysed thematically following the steps or stages below. Firstly, each audio-recorded interview was transcribed verbatim. This was done immediately; meaning the same day the interview was conducted. Secondly, each transcript was read at least twice by the researcher to familiarize

himself with its contents. Thirdly, each transcript was coded thematically, and similar codes were subsequently grouped together. Fourthly, each group of similar codes was assigned a name to reflect the generic meaning of the codes. The assigned name was what was referred to as a major theme, and its constituents were referred to as sub-themes. The data analysis generated 29 sub-themes that were clustered under the 7 major themes. These major themes and their constituents or sub-themes are illustrated in table 3.1 below. These major themes and sub-themes are discussed in the result chapter of the study.

Table 3. 1: The major theme and sub-themes of the study

Major themes	Constituents or sub-themes
Functionality of the programme of MDR-TB	• Patients' and community knowledge on MDR-TB • Health system's support for the programme of MDR-TB • Patient linkage to a continuum of care • Recognition for caregivers
Decentralization of the directly observed treatment (DOT) support	• Distance from service centre • Engagement of community health extension workers
Management of adverse drug reactions	• Impact of adverse drug reactions, • Ancillary drugs, • Follow up services, • Knowledge of caregivers, • Prompt emergency care • Adherence challenges
Socio-economic support	• Poverty, • Socio-economic impact of MDR-TB, • Adequacy of support, • Quality of support • The use of available resources
HIV and MDR-TB co-management	• Service integration, • Caregivers' capacity • Unfavourable treatment outcomes
MDR-TB infection prevention and control	• Health facility level risk of infection • Patients' household level risk of infection • MDR-TB disease transmission among contacts
Patients' perceived quality of care and patients' satisfaction	• Patient engagement in treatment decision making, • Emergent medical conditions, • Caregivers' responsiveness, • Service set ups, • Communication between the patient and their caregivers • Compassionate care

3.10. Quality of the study

3.10.1. Quantitative component: validity and reliability

3.10.1.1. Validity

Validity of research is the extent to which an instrument measures what it is actually supposed to measure (Creamer 2018:84) or the extent to which a concept is accurately measured (Heale & Twycross 2015:66). Validity addresses the question of how well we measure social reality using our constructs about it (Newman 2014a: 212). Validity ensures that the evidence gathered supports the type of inferences that are intended to be drawn from the measurement (Boslaugh 2013:12).

There are several types of validity, but the focus here is on internal and external validity. Internal validity is concerned with the extent to which explanations can be made about the observed relationship between the independent and the dependent variables of interest. Internal validity entails the elimination of variations in scores on the dependent variables that are unrelated to the effects of the independent variable. (Crano et al 2015:27-32).

External validity is the extent of generalizability that the results can be applied to other participant groups in different settings and different ways of operationalizing the conceptual variables (Lancaster 2005:163). It demonstrates that the same independent variable used in previous works has a similar effect on the dependent variable of interest in a different context and with different study participants (Crano et al 2015:142.

In this study, efforts were made to ensure that the research tool accurately measures the variables under investigation. The steps taken to ensure validity of this study are described below:

3.10.1.2. Development of the study instrument

The development of an instrument used in a study was guided by a salient theoretical framework and available literature. This is because validity is inextricably tied to theory (Barry, Chaney, Stellefson & Chaney 2011:99). In this study, certain steps were taken to make sure that the scores produced by the instrument are valid. As such, the content of the instrument was sketched and built in a way that it has a logical link with the objectives of the study and also it can appropriately cover all the dimensions of the construct under investigation. Efforts were also made to ensure the logical flow or coherence of the items in the instrument used. Clear and easy to understand wording was used to state each single question in which double-barrelled questions were avoided. The implementation of each section of the instrument was guided by clear instructions on how to implement it. Screening questions were used as a means of transition from one section of the instrument to the other section.

Once developed, the instrument was serially reviewed by the researcher's supervisor and other professionals who had sound concept on research methods and also who had the expertise in the construct under investigation (that is, experienced in the programmatic management of drug-resistant tuberculosis). The comments obtained from experts were incorporated to make sure that the tool is sensitive to measure what it meant to measure and also is understood in the same way if used by different experts. In this way, efforts were made to maximize the appropriateness of the instrument used to measure the constructs and variables under investigation.

3.10.1.3. Training of data collectors

To make sure that the study questionnaire is understood by all the data collectors involved in the data collection process, data collectors were given a two-day training. The trained data collectors were also part of the process of pilot testing the questionnaire. Data collectors were also re-oriented on the final tool which incorporated comments gathered so that they get familiar with updates in the content of the questionnaire and how to apply it.

3.10.1.4. Monitoring of the data collection process

In this study, the principal investigator monitored the whole process of the data collection. The principal investigator took the lead responsibility in making sure that the data collection process was smooth and was implemented as planned. Specific actions taken in the field included ensuring the completeness of the individually filled in questionnaires; they were checked on the spot. When there were incomplete values in a filled in questionnaire, these were addressed immediately by revisiting the source of that particular data. It was ensured that written values were legible. Then when it was confirmed that a filled in questionnaire was complete, it was coded and filed for subsequent use.

3.10.1.5. Reliability

Reliability is the extent to which a questionnaire or a test or a procedure consistently produces the same results that it is measuring on repeated trials. Reliability basically refers to the consistency of results obtained in research (Boslaugh 2013:10).

There are three major attributes of reliability. The first of these attributes is the internal consistency or the homogeneity of the study instrument. Internal consistency focuses on the extent to which all the items in the study instrument measure the same construct under investigation. The second is stability, which deals with consistency of the scores obtained on repeated testing using the instrument. The third is equivalence which deals with the consistency of the scores among the different sections of the instrument (Heale & Twycross.2015:66-7).

3.10.1.6. Steps taken to ensure reliability of the quantitative component of the study

Steps were taken to ensure the reliability of the quantitative part of the study. Every construct under investigation and its sub dimensions were clearly conceptualised and its clear and unambiguous theoretical definition was developed. This helped to eliminate interfering information so that each measure clearly indicated one and only one concept. Moreover, multiple questions were asked per each construct of interest. Use of multiple indicators per a construct helped to make the study tool more stable and reduce the chance of systematic error from using single indicator per construct of

interest (Newman 2014b:141). Furthermore, reliability of the instrument used was tested using the Cronbach's alpha statistical test. A research instrument is said to be reliable if it consistently measures the construct that it is intended to measure. Statistically, the Cronbach's alpha coefficient is the commonly used statistical test for establishing the reliability of an instrument. Cronbach's alpha is an index of the internal consistency (reliability) of a set of items in an instrument (Gaur & Gaur 2009:134).Cronbach's alpha is a hypothetical value that would be obtained if all of the items that could constitute a given instrument were available and randomly combined across a large number of tests of equal size (Crano, Brewer & Lac 2015:447). Reliability of an instrument is acceptable if the value of its Cronbach's alpha coefficient (α) is equal to or greater than 0.7 to 0.8. For the instrument used in this study, the value of the Cronbach's alpha coefficient (α) was 0.72, that is (α=.72, p=0.001). The value of the Cronbach's alpha coefficient for the instrument used in this study was greater than the proposed acceptable value (Field 2009:673-5).

3.10.1.7. Other measures taken to ensure reliability of the quantitative component of this study

Before the main data collection, a pilot test was conducted on patients with MDR-TB treated in one referral hospital in the Oromia Region of Ethiopia rather than the two referral hospitals selected for the study. This activity created an opportunity to evaluate the appropriateness of the instrument used for the quantitative component of the study for the researcher and the study team. The experience gained from the pilot testing was discussed among the team. Concerns in the level of the clarity or any ambiguity in the administration of the data collection instrument was fully addressed. Moreover, the data obtained from the pilot test was entered into SPSS version 23 and the outcome of the analysis was used in the refinement of the questionnaire.

Experts, other than the principal investigator, were involved in checking the process of data analysis. In addition, an experienced statistician and a public health researcher who were not part of the whole process of this research endeavour, were invited to check the process of data analysis. The comments and input provided by the two experts were used in the process of data analysis and report writing.

3.10.2. Qualitative component: trustworthiness

Trustworthiness of a qualitative data is the degree to which the results are credible, transferable, confirmable and dependable (Andrew & Halcomb 2009:122).

3.10.2.1. Credibility

Credibility is the extent to which the methods used engender confidence in the truth of the data and the researcher's interpretation of the data. Credibility deals with the question of how congruent the results of a study are with reality (Edmonds & Kennedy 2017:324).

3.10.2.2. Steps taken to ensure credibility in this study

3.10.2.2.1. Triangulation

Triangulation is verification through the use of multiple sources of data about the same phenomena. It is the use of data from different or multiple sources used to justify the themes. Such multiple sources of data may include the use of individual interviews, interview notes, focus groups, photos, observations and documents (Creamer 2018:3). In this study, data were obtained from different categories of participants. In-depth interviews were conducted with caregivers (physicians and nurses) and with patients with MDR-TB. Interview data were audio recorded and transcribed verbatim. Notes were taken during interviews where data were captured on the feelings and the experiences of the study participants. Data from multiple sources were used to make sure that emerging themes were established based on converging different sources of data or different perspectives of the segments of the study participants. The data from different sources were analysed separately and then compared.

3.10.2.2.2. Member checking

Member checking is presenting recorded data or interviews or a draft result of the research to persons from whom the information was obtained and asking them for comments and corrections (Stake 2010:136). This is the moment in which the views and the perspectives of the study participants are solicited to ensure the credibility of the study results and the interpretations made regarding the results obtained (Creswell 2012: 259; Creswell 2007:208). In this study, the researcher made sure that the

information he captured reflects the views and opinions of the study participants. For this, the principal investigator summarized what was discussed at the end of each interview. Then each participant was asked if what the researcher captured actually matches the intentions and opinions of the participants. Moreover, transcripts were given to some literate participants and they were asked if what the researcher captured matches their opinions. In the process of the data collection preliminary scanning of the emerging themes were made. In such instances some themes were presented to same participant and clarification was asked when appropriate.

3.10.2.2.3. Peer scrutiny

Peer debriefing is the opportunity for a research endeavour to be scrutinized by peers and the academic colleagues. This entails the use of their questions and feedbacks during the whole process of the qualitative inquiry to enhance accuracy of the construct under scrutiny (Creswell 2008:192). In this study, two persons (debriefers) were located and the emerging themes and the draft results of the study were frequently debriefed with them. The debriefers had experience in social research. The feedback, questions and the views of these debriefers were taken into consideration to widen the vision of the principal investigator in the interpretation of the construct under investigation.

3.10.2.2.4. Frequent debriefing with supervisor

Both the transcriptions and the emerging themes were communicated to the supervisor of the study. As such, the detailed audit made by the supervisor and the comments given were used to enhance the accuracy of the interpretations made on the construct under scrutiny. Moreover, the preliminary results of the qualitative data were communicated to the supervisor who thoroughly revised the draft results. Comments provided by the researcher's supervisor on improving the credibility of the results were used to enhance the vision and accuracy of the construct. This was to make sure that the results are data driven and the inferences made are credible.

3.10.2.2.5. Thick description of the phenomena under scrutiny

Thick description is the provision made to make sure that what a researcher defines actually conveys the actual situation that is investigated (Creswell 2012:448). In this study, a summary of the results and the interpretations made were presented for each theme. Then with the attempt to keep the data rooted in the participants' own words, each of the summaries made was illustrated by using direct quotations or excerpts from what the participants were actually providing.

3.10.2.2.6. Honesty and integrity

Researchers are required to make sure that a research attempt is conducted according to the acceptable standards of practice and without fraud (Walliman 2011:43-5; Blaikie 2010:31). To get thorough and correct answers to the interview questions posed to the participants, researchers are required to ensure the willingness of the participants to provide genuine answers without fear (Polit & Creswell 2012:80).

3.10.2.2.7. Ensuring honesty and integrity in this study

In this study, the process of participant selection was made in which participants were honestly informed on what was expected of them and their right to refuse participation at any point in the process of the interviews (see annex IV) was highlighted. As such, when approached, each participant was told that he or she had the right to refuse participation if he or she could not contribute data and talk of their experiences without fear. During data analyses and reporting, a full range of the results (both positive and negative) was reported on as obtained from the participants.

3.10.2.2.8. Development of early familiarity with the study setting

Acquiring an intimate understanding of the study setting is the process of maximizing the advantage of personal insight to understand the inner feelings and life perspectives of the study participants in real social life. It is not being sloppy about data collection nor use of evidence selectively but it is used to influence professional judgments (Neuman 2014:170). In this study, familiarity with the setting was obtained through visiting the study sites before data collection began. The principal investigator and the trained data collection assistant visited the Adama and Nekemte Referral hospitals and talked to the Chief Executive Officers of the two hospitals. Preliminary knowledge was

obtained regarding the study setting, the living conditions of the patients with MDR-TB and the routines in the implementation of the MDR-TB programme at the two hospitals. Moreover, during the whole time of data collection, the researcher attended and facilitated every event of the interviews made with patients and their caregivers. In this way, the familiarity with the study setting helped in the process of data collection, analysis and report writing.

3.10.2.3. 3.10.2.3. Confirmability

Confirmability is objectivity. It is the degree to which the results are derived from the experience of participants and their context and not from the researcher's own biases (Neuman 2014:218). Confirmability is one of the validation strategies for qualitative inquiry. It deals with ensuring that the results of a study are meaningful and applicable in terms of the study participants' own experiences and their understanding of the phenomena under investigation (Andrew & Halcomb 2009:129).

3.10.2.4. Steps taken to ensure confirmability in this study

In this study, all the interpretations and the conclusions reached were supported by direct quotations of the excerpts from the raw data and as explained by the participants of the study. The complete verbatim transcript produced from the audio-recorded qualitative data is made available for reference.

3.10.2.5. Transferability

Transferability is the degree to which the results of a qualitative study are transferred to other settings. That is, it deals with the applicability of the qualitative results to similar settings (Heyvaert, Hannes, Maes & Onghena 2013:7).

3.10.2.6. Steps taken to ensure transferability in this study

To ensure transferability of the study results, attention was given to data saturation and to the description of the original context of the data. The detailed description is provided to enable readers to decide on the extent of the applicability of the results of this study to other settings.

Through the member checking activity implemented, the verbatim transcripts were shared with interviewees to get their approval and to make sure that what was captured in the study, reflects their perspectives and the actual context. The preliminary themes and results were also communicated to the participants to make sure that the results and the interpretations made were reflective of the views of the participants.

3.10.2.7. Authenticity

Authenticity is fairness. It is the criterion, which deals with the degree to which data presents a balanced perspective of the participant's constructions of reality and the underlying values (Hesse-Biber & Johnson 2015:248).

Qualitative studies are more interested in achieving authenticity than realizing a single version of truth. Authenticity means offering a fair, an enriched, honest and balanced account of social life from the viewpoint of the people who live it everyday. It achieves this through the use of data from various sources including photographs, notes and the verbatim transcripts of the interviews (Neuman 2014:218).

There are five authenticity criteria. The first is fairness. Fairness deals with the researcher's effort to present the experiences and the views of participants in a balanced way that can be honoured by involved groups. The second form of authenticity is ontological authenticity. This deals with making sure that reality is constructed exactly as it is experienced by those who live it. The third form of authenticity is the educative authenticity. This form of authenticity deals with the improved understanding of the constructions of others and understand how such constructions are rooted in the differing values of those others. The forth form of authenticity is catalytic authenticity. According to catalytic authenticity, achieving

increased understanding of a reality is not sufficient. Indeed, inquiry must stimulate action. The fifth form is tactical authenticity which deals with empowering those who have the stake to have the opportunity to control over what is understood and for it to be translated to action (Yang & Miller 2008:159).

3.10.2.8. Steps taken to ensure authenticity in this study

The data from the various sources were presented in a mutually reinforcing and interlocking manner. Moreover, the results and the interpretations made were presented back to the study participants. Participants were asked if they agreed with the results and the interpretations made by the researcher. All the interviewees agreed with the authenticity of the data. They also agreed that the interpretations made represent their views and perspectives and they did not add new any information to the data and the interpretations made. Added to this, effort was made to make thick and rich descriptions of the everyday life experiences of the study participants and all the contextual aspects of the research settings. The involvement of the different categories of participants (patients and healthcare workers) was to ensure representation of the multiple realities of what was under investigation. Thus, member checking was applied to ensure that the results fit the experiences and the perspectives of the study participants. One of the aims of this study was to develop a model for enhancing the management of patients with MDR-TB. This model will contribute to social change in the area being investigated.

3.10.2.9. Dependability

The dependability of a qualitative result is the degree to which the results are consistent and stable. The audit trails ensure that the findings of the study are consistent and repeatable (Edmonds & Kennedy 2017:324).

3.10.2.10. Steps taken to ensure dependability

In this study, the dependability audit was conducted through an external auditor. The external auditor had multiple years of experience in the field of social research. He also had experience in the programme of MDR-TB. He was not directly involved in any part of the current research process.

The external auditor explored the processes followed in data collection, data analysis and the conclusions reached. He confirmed that the results of the study, the interpretations made and the conclusions drawn from the findings are supported by the data collected for the study.

3.11. Ethical considerations

3.11.1. Permission to conduct the study

Ethical approval of the research proposal was obtained from Higher Degrees Committee (DHDC) of the Department of Health Studies at UNISA (annexure 3.1.). Likewise, a support letter was obtained from UNISA, Regional Learning Centre in Ethiopia, at Akaki Campus (annexure 3.2).

Permission to access the targeted hospitals was obtained from Oromia Region Health Bureau, the Department of Public Health Emergency Management and the Health Research Core process (annexures 3.3-3.4). Next, permission on access to patients with MDR-TB, caregivers for MDR-TB and patient records was obtained from the Chief Executive Officers (CEOs) of Adama and Nekemte Referral Hospitals. Subsequently, access to patients with MDR-TB was obtained through informed permission from the caregivers for patients with MDR-TB in each hospital.

3.11.2. Informed consent

Informed consent is an essential requirement and it is an integral part of clinical and public health researches involving human subjects (Council for International Organizations of Medical Sciences (CIOMS) 2016:72).

In this study, the information sheet (see annexure 4) was prepared and used to ensure that participation was entirely based on informed consent. The contents of the information sheet were read to each patient. Based on the information sheet, an explanation was advanced on the objectives of the study and the need for participation by patients with MDR-TB and their caregivers.

It was explained that participation of patients with MDR-TB and their caregivers was important to get data on their feelings and experiences on the programme of MDR-TB

and the services provided for patients. In addition, data generated would be used to guide and provide evidence informed decision making data regarding the programmatic management of drug-resistant tuberculosis in referral hospitals found in the Oromia Region of Ethiopia and other similar hospitals found in Ethiopia.

It was made clear that all the data collected from patients and their caregivers were anonymous. This means that participants were not asked about their personal identifying information like name and address. Furthermore, confidentiality of responses given was adhered to. This means that information collected was used only for answering the research question under investigation. The information would not be shared with anyone else and would not be analysed and reported on in conjunction with participants' personal identifiers. To that end, participants were told that participation was entirely voluntary and they had the right not to participate in the study. It was made clear that patient's decision not to be part of the study would not have any negative impact on the care and services that the patients obtained from the hospitals. As such, patients with MDR-TB and their caregivers had the full right to withhold participation without any precondition.

3.11.3. Ethical considerations of using patient records as the source of data

Access to records of patients with MDR-TB from registers and patient charts was obtained through permission from hospital management and the caregivers for patients with MDR-TB. No data were collected on patient identifiers. Instead, codes were used to identify each filled in questionnaire. Confidentiality of all data collected was kept or adhered to.

3.11.4. Compensation for study participants

In any research endeavour, compensation or an incentive is considered as a token of appreciation rather than a payment for the participant's efforts in participating in the research. Every effort should be made to prevent the compensation from inducing any willingness to participate in the study or prevent it from being considered as a reward for the task of participating in the study (Goodwin 2010:59).

In this study, patients with MDR-TB who came for their scheduled monthly follow up services at Adama and Nekemte referral hospitals participated in the in-depth interviews. Some of the patients who voluntarily sacrificed their time to provide responses to the interviews were warned that they could miss their buses. That might lead to these patients having to pay for snacks due to the delay until late in the afternoon before returning to their home areas or they may be exposed to paying extra transport fees for using inter-town taxies.

In this study, the issue of compensation for a missed transport schedule resulting in the potential financial risk due to the time that participants spent with the researcher, was not disclosed until the participant's informed consent was obtained and the interviews were completed. After completion of the in-depth interviews with each participant, the issue of compensation for potential financial risk was discussed with the participants themselves and the hospitals nurse focal point for the MDR-TB services. To avoid information sharing among participants, the compensation was given while the participant exited from the facility. Twelve of the total participants of the interviews received 50 Ethiopian Birr (equivalent to 1.8 USD at that time). For the remaining participants, there was perceived extra financial risk incurred by the patient that needed compensation. This level of compensation was only nominal and served to compensate for perceived real financial risk that a participant could incur. No compensation was needed for caregivers who volunteered to participate in the interviews.

3.12. Summary

This chapter illustrated the principles, ideas and procedures on which this research endeavour was based. The chapter summarized the different assumptions or research paradigms and the research design used in the study. It indicated that the study employed facility based, analytical and a concurrent mixed methods design. The study was predominantly quantitative in design which is supplemented by a concurrent qualitative inquiry. The chapter also depicted the research setting and population of the study. Moreover, it indicated procedures used for sample selection, instrument development, data collection and its management. Finally, the chapter presented a summary of the procedures used to ensure validity and reliability of the research results.

This chapter describes the philosophical and methodological assumptions used in this study. It also describe the specific research design and methodology that guided this research endeavour. The next chapter (chapter 4) will present data analysis and the result of the research.

Chapter 4: Research results

4.1. Introduction

In the preceding chapters, the background to the research problem and the scope of the research problem investigated in this study were presented. The literature review and the methodological procedures used to implement the study were also presented in preceding sections. The results of the study are presented in this chapter of the study.

4.2. Results for the quantitative component of the study

4.2.1. Socio-demographic characteristic of study participants

From the total of 136 (100%) patients with MDR-TB included in the study, 74 (54%) were male while 62 (46%) were female patients with MDR-TB (see figure 4.1). According to figure 4.2 and table 4.1, the majority of patients were found to be in the productive age group with 128 (94%) of the patients being in the age group of 15-64 years. Similarly, 28/30 (93%) of the total deaths from MDR-TB occurred in the same age group of 15-64 years. About 4 (3%) of patients with MDR-TB were aged less than 15 years of age while 4 (3%) of them were aged 65 years and above. The mean age of the study participants (Mean ± SD) was 32.12 ± 12.53. The actual age range of the study participants was 4-73 years (see figure 4.2).

Table 4.1 shows that the majority, 70 (53%) of patients were self-employed. This was followed by 46 (35%) who were not employed. Seven (5%) of patients were formally employed while 9 (7%) of the patients were in the other response category comprising mainly of students and housewives. In this study, the interviews conducted with patients with MDR-TB revealed that, 53% self-employment was described as employment in the informal labour workforce with minimum daily wages.

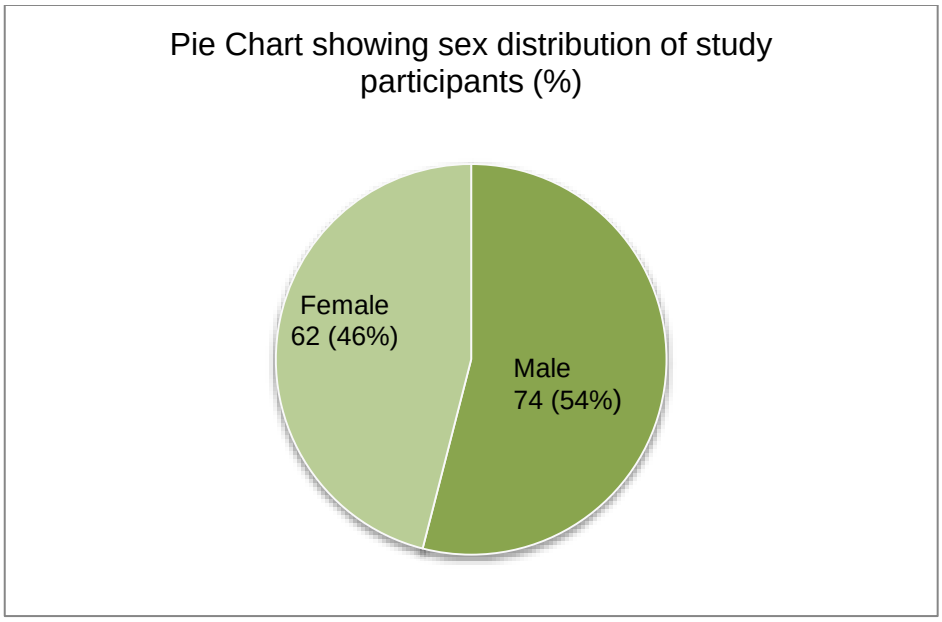


Figure 4. 1: Sex distribution of study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=136)

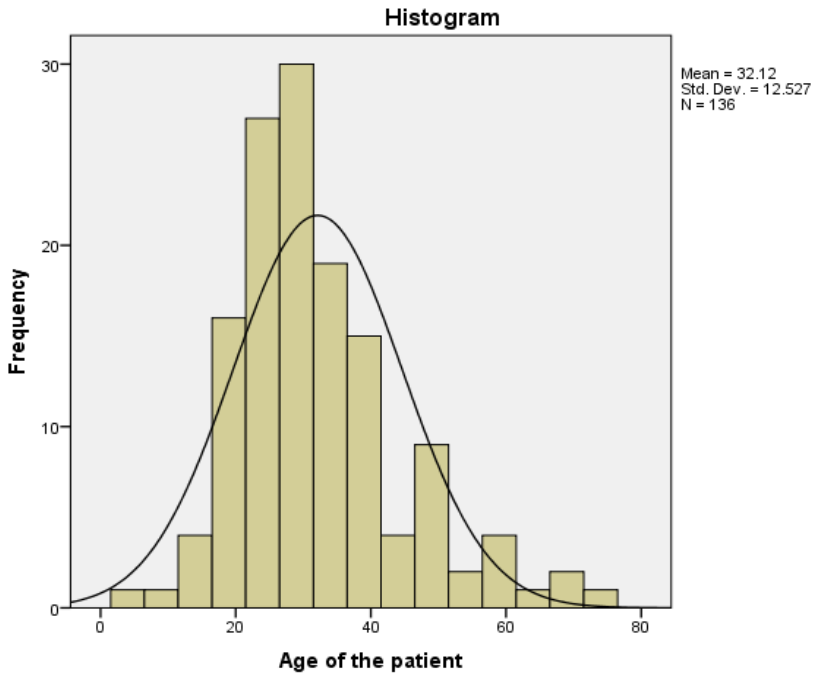


Figure 4. 2: Age distribution of the study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=136)

Table 4. 1: Socio-demographic and socio-economic characteristic of the study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=136).

Parameter	***N (%)***
Sex (n=136):	
Male	73 (54)
Female	63 (46)
Age category (n=136)	
<15 years	4 (3)
15-44 years	110 (81)
45-64 years	18 (13)
>/=65 years	4 (3)
Patients' employment status (n=132)	
Formally employed	7 (5.3)
Self employed	70 (53)
Unemployed	46 (35)
Other	9 (7)

4.2.2. Clinical characteristic of the study participants

4.2.2.1. Type of the MDR-TB cases and patients' registration groups

At registration, patients with MDR-TB who were included in this study were grouped based on the type of tuberculosis they suffered from, their previous treatment history and the outcome of their latest tuberculosis treatment. Table 4.2 shows that the majority of the patients with MDR-TB, about 134 (98%) were bacteriologically confirmed pulmonary MDR-TB cases. One patient (1%) was bacteriologically confirmed extra-pulmonary MDR-TB and one patient (1%) was clinically diagnosed as an extra-pulmonary MDR-TB case.

The analysis of the patients' registration group revealed that the majority, 90 (66%) of the patients, were diagnosed with Rifampicin Resistant TB or MDR-TB after the failure of the re-treatment regimen with the first-line tuberculosis treatment regimen. This was followed by 17 (13%) patients diagnosed with MDR-TB after the failure of treatment with the new standard 6-month regimen with first-line anti-tuberculosis drugs. Fourteen (10%) of patients were those registered for treatment after a relapse, while 11 (8%) were new cases of RR/MDR-TB who did not have any history of treatment with anti-tuberculosis drugs. About 4 (3%) of the patients were those diagnosed among patients returning after being lost to follow ups. Only 1 patient had a history of treatment with a regimen containing second-line anti-tuberculosis drugs. This patient was a patient who returned after being lost to follow ups while on treatment for MDR-TB.

4.2.2.2. Drug-resistance pattern of the patients with MDR-TB

At the baseline from the total patients included in this study, 89 (65%) were diagnosed as Rifampicin Resistant (RR) cases by the GeneXpert machine. About forty-seven (35%) of patients were diagnosed as MDR-TB cases. The drug-susceptibility test result both for rifampicin and isoniazid is obtained from the culture and drug-susceptibility test. As a result, all patients registered as MDR-TB had a documented drug-susceptibility test result for both rifampicin and isoniazid anti-tuberculosis drugs. Thirty-four (26%) of the patients with a documented HIV test result were co-infected with HIV/AIDS. One hundred and thirty four (98%) of the total tuberculosis cases were pulmonary, while 2 (2%) were extra-pulmonary cases of tuberculosis. From the total

(n=132) of patients with a documented baseline sputum microscopy test, 27 (21%) were sputum smear negative while 105 (79%) were sputum smear positive patients with MDR-TB. An analysis of the initial bacillary load at diagnosis (n=132) revealed that the initial bacillary load for 59 (45%) patients was scanty, moderate for 41 (31%) and high for 5 (4%) patients. From the total patients documented, diagnostic radiology was used for 37 (27%) of the patients. For forty one (30%) of the patient's, diagnostic radiography was not used and instead, diagnosis was made based on other diagnosis tools. For fifty-eight (43%) of patients, there was no evidence on the status of the use of diagnostic radiography.

4.2.2.3. Drug-susceptibility test status of the patients to tuberculosis drugs

Table 4.2 shows that at diagnosis, 135 (99%) patients had a drug-susceptibility test result for Rifampicin and were resistant to Rifampicin. Only fifty-eight (43%) of the total 135 patients had a drug-susceptibility test result for Isoniazid and were resistant to Isoniazid. Three (2%) patients had a drug-susceptibility test result for Streptomycin and were resistant to the drug. All patients (n=136) did not have a drug-susceptibility test result for Ethambutol and Pyrazinamide drugs. Furthermore, no drug-susceptibility test results were available for any of the second-line anti-tuberculosis drugs used to treat MDR-TB.

Scholars, cited that the limited availability of diagnostic drug-susceptibility test service, leads to the use of an inappropriate regimen which in turn leads to the further amplification of resistance. In view of such recommendations, the availability status of diagnostic drug-susceptibility test for patients with MDR-TB of those included in this study, seems to be sub-optimal (Dobler, Korver, Batbayar, Nyamdulam, Oyuntsetseg, Tsolmon, Surmaajav, BayarjargalB & Marais 2015:1451; Minion et al 2010:941).

4.2.2.4. Status of the baseline co-morbidity associated with MDR-TB

As shown in table 4.2, from the total of 133 (n=133) patients for whom data was available on any co-morbidity with MDR-TB at the baseline, 41 (31%) had some form of co-morbid condition at baseline. From the total of 41 MDR-TB associated co-morbidities at baseline, 34 (83%) of the co-morbidity at baseline was due to co-infection with HIV while 5 (12%) was co-morbidity with diabetes mellitus. This was followed by other types of co-morbidities 2 (5%) including cardio-vascular diseases, kidney diseases, co-pulmonale and anemia. Furthermore, the study revealed that 87 (64%) of the patients with MDR-TB had a body mass index (BMI) of less than 18.5kg/m2, indicating the presence of malnutrition as a co-morbid condition with MDR-TB.

Table 4. 2: Clinical characteristics of the study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=136).

Parameter	***N (%)***
Patients' drug-resistance type at diagnosis (n=136)	
Rifampicin resistant tuberculosis (RR-TB)	89 (65)
MDR-TB	47(35)
HIV test result (n=131):	
HIV positive	34 (26)
HIV Negative	97 (74)
Presence of co-morbidity at baseline (n=133)	
Yes	41(31)
No	92 (69)
Type of co-morbidity at baseline (n=41)	
HIV/AIDS	34(83)
Diabetes mellitus	5 (12)
Other	2(5%)
Was sputum smear used for diagnostic (n=135)	

Yes	133 (98)
No	2 (2)
Was GeneXpert used for diagnosis (n=136)	
Yes	86 (63)
No	50 (37)
Was LPA used for diagnosis (n=135)	
Yes	49 (36)
No	86 (64)
Was culture used for diagnosis (n=135)	
Yes	21 (16)
No	114 (84)
Site of the TB disease (n=136)	
Pulmonary	134 (98)
Extra-pulmonary	2 (2)
Type of the TB case (n=136)	
Bacteriologically confirmed pulmonary TB	134 (98)
Bacteriologically confirmed extra-pulmonary TB	1 (1)
Clinically diagnosed extra-pulmonary TB	1 (1)
Result of diagnostic sputum smear examination (n=132)	
Smear positive	105 (79)
Smear negative	27 (21)
Sputum bacillary load reported at diagnosis (n=132)	
No AFB seen	27 (20)
Scanty	59 (45)
Moderate	41 (31)
High	5 (4)

4.2.2.5. Clinical management of patients with MDR-TB

4.2.2.5.1. Approaches to the clinical management of patients with MDR-TB

The study revealed that all patients (n=136) were treated using the WHO recommended standardized treatment regimen for MDR-TB which is 8 (Z-Cm6-Lfx–Pto (Eto)–Cs for the intensive phase and 12 (Z-Lfx–Pto (Eto)–Cs for the continuation phase.

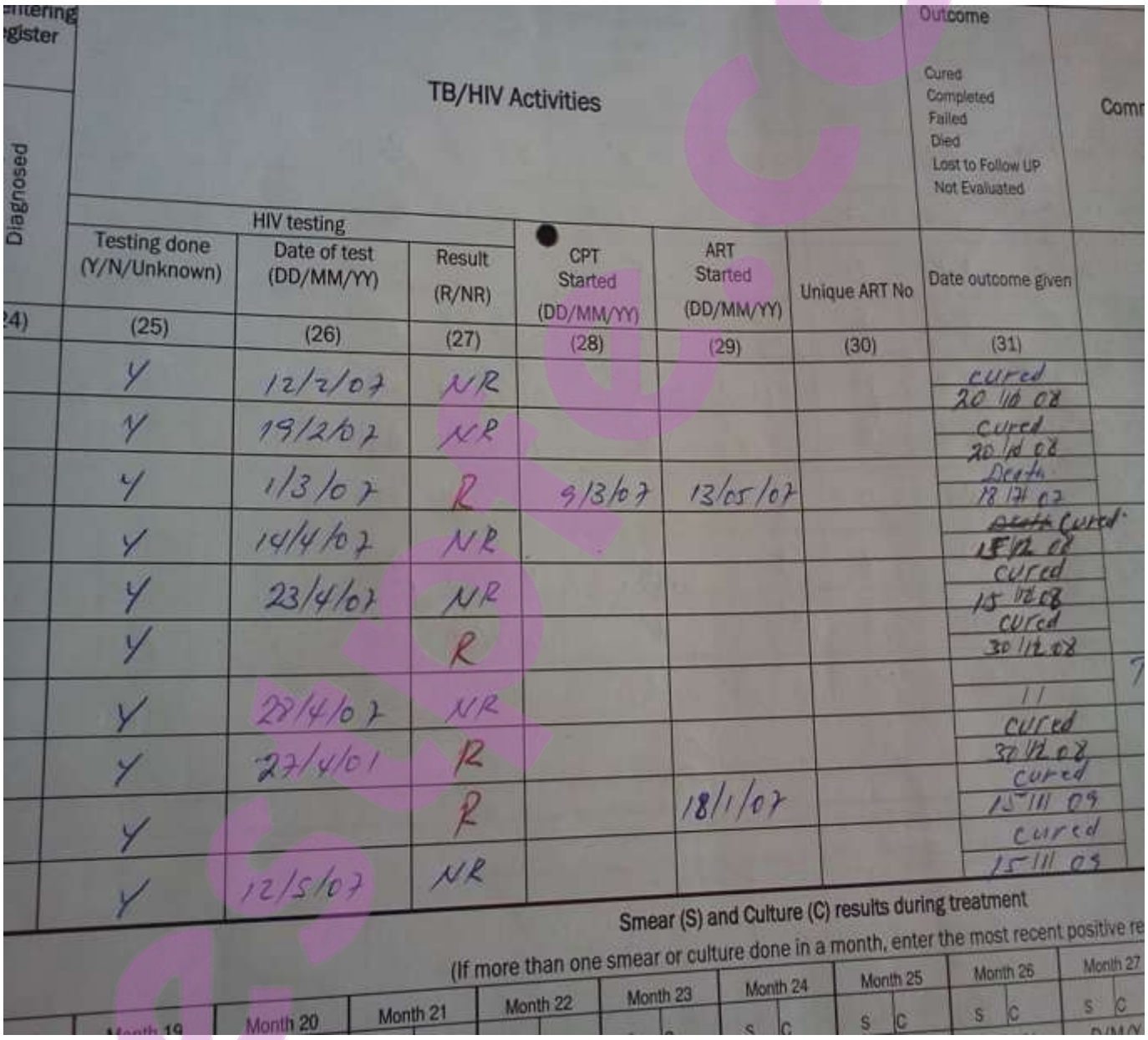
Caregiver participants in the qualitative in-depth interviews, mentioned that an injectable capreomycin (second-line tuberculosis drug) is given six days per week. The MDR-TB treatment regimen given for all 135 (99%) of patients contained four second-line anti-tuberculosis drugs not previously used in the patient's tuberculosis treatment regimen.

An analysis of the number of total tablets taken per day by a patient with MDR-TB showed that 32 (23%) patients were taking 12 tablets or less per day. Fifty seven (42%) of patients took 13 to 14 tablets per day while 46 (34%) of patients took 15 or more tablets of the second-line anti-tuberculosis daily.

The in-depth interviews with caregivers revealed that there was no standard registration system for total tablets given to treat adverse drug-reactions from second-line drugs. Therefore, the question asked in order to capture the average number of daily tablets that a patient with MDR-TB took could only be captured from the number of tablets of second-line drugs included in the standard MDR-TB treatment regimen. This may imply that patients experiencing adverse drug reactions may be taking more tablets than the specific question captured in this study. One hundred and sixty six (85%) of the patients who passed the treatment phase from intensive to continuation phase were put on the WHO recommended standard treatment regimen of 12 (Lfx-Eto-Cs-Z) for the continuation phase.

4.2.2.5.2. Status of the MDR-TB and HIV/AIDS co-management

From the total number of patients enrolled to treatment for MDR-TB at the two hospitals, 131 (96%) of the patients had a documented HIV test result. From total number of those tested, 34 (26%) were positive with HIV, which means that 26% of the patients with MDR-TB were co-infected with HIV/AIDS. As depicted in the figure 4.3 that follows, 4 out of 10 (40%) of the patients with MDR-TB who were registered on a single page of the unit MDR-TB register were reactive (**R**) for HIV.



Diagnosed	TB/HIV Activities: HIV testing: Testing done (Y/N/Unknown)	Date of test (DD/MM/YY)	Result (R/NR)	CPT Started (DD/MM/YY)	ART Started (DD/MM/YY)	Unique ART No	Outcome: Date outcome given
24)	(25)	(26)	(27)	(28)	(29)	(30)	(31)
	Y	12/2/07	NR				cured 20/10/08
	Y	19/2/07	NR				cured 20/10/08
	Y	1/3/07	R	9/3/07	13/05/07		Death 18/12/07
	Y	14/4/07	NR				~~Death~~ Cured 15/12/08
	Y	23/4/07	NR				cured 15/12/08
	Y		R				cured 30/12/08
	Y	28/4/07	NR				11 cured 30/12/08
	Y	27/4/01	R				cured 15/11/09
	Y		R		18/1/07		cured 15/11/09
	Y	12/5/07	NR				

Smear (S) and Culture (C) results during treatment

(If more than one smear or culture done in a month, enter the most recent positive re

Month 19	Month 20	Month 21	Month 22	Month 23	Month 24	Month 25	Month 26	Month 27
					S C	S C	S C	S C

Figure 4. 3: Status of MDR-TB and HIV co-infection among patients with MDR-TB treated at the two referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016.

The study revealed that from all (n=31) patients with documented evidence on tuberculosis and HIV co-management, 30 (98%) had documented evidence that they were given cotrimoxazole preventive therapy and anti-retroviral treatment. However, none of the HIV and MDR-TB co-infected patients had documented T–lymphocyte cell bearing (CD4) count at the initiation of treatment for MDR-TB.

4.2.2.6. Adverse reactions from second-line anti-tuberculosis drugs

4.2.2.6.1. Prevalence of adverse drug reactions from second-line drugs

From the total number of patients included in the study, complete data on adverse drug reactions from second-line drugs were retrieved for 91 (67%) patients. All the 91(100%) patients with data on adverse drug reactions from second-line drugs experienced at least one episode of some form of adverse drug reactions from second-line drugs in the course of their treatment for MDR-TB. The adverse drug reactions involved major body organs. The median number of the adverse drug reactions from second-line drugs per patient included in this study was found to be four.

From the total of 91 patients, 31(34%) of them experienced five or more episodes of adverse drug reactions from second line drugs. Twenty-two (24%) of the patients experienced two episodes of adverse drug reactions while 14 (15%) of them experienced three episodes of adverse drug-reactions from second-line drugs. Twelve (13%) of the patients experienced four episodes of adverse drug reactions and same 12 (13%) of them experienced one episode of adverse drug reactions from second-line drugs.

4.2.2.6.2. Occurrence of adverse drug-reactions by body organs involved

Systemic differentials for the occurrence of adverse drug reactions from second line anti-tuberculosis drugs revealed that, from the total of 91 patients, 73 (80.2%) of them experienced at least one episode of adverse drug reactions involving the gastro-intestinal tract. Analysis of the gastro-intestinal tract related adverse drug reactions by site of involvement of the gastro-intestinal tract, revealed that from the total of 73 patients who experienced gastro-intestinal tract related adverse drug reactions, 34

(46.6%) experienced nausea and vomiting and 51 (70%) experienced gastritis including diagnosis with peptic ulcer disease.

Neurological related adverse drug reaction was also found to be the second most common adverse drug reactions in which 35 (38.5%) of the patients developed this type of adverse drug reactions from second-line drugs. Most common neurological adverse drug reactions found among the patients included in this study were peripheral neuropathy and headache. The 35% prevalence of the neurologic related adverse revealed in this study, was higher than the 6% neurologic related adverse drug reactions reported by Akshata et al (2015:31).

The study also revealed that musculoskeletal related adverse drug reactions from second-line drugs was the third common adverse drug reaction among patients with MDR-TB. As such, 26 (28.6%) of the patients experienced musculoskeletal related adverse drug reactions from second-line drugs. In the same way, 24 (26.4%) of patients developed cardio-vascular related adverse drug reactions from second-line drugs. 13 (14.3%) patients experienced electrolyte disturbances while 11 (12%) of the patients developed psychiatric related adverse drug reactions.

The 12% psychiatric disorder revealed among patients with MDR-TB in this study is much higher than the 1.6% reported by Akshata et al (2015:31) but it is similar to the 13% prevalence of psychosis reported by Bloss et al (2010:277) among patients with MDR-TB in Lativia. Moreover, 9 (10 %) patients experienced vestibular (ear) related adverse drug reactions while 7 (7.7%) developed dermatologic related adverse drug reactions. Five (5.5%) and 3 (3%) of patients developed eye and immune related adverse drug reactions respectively.

Irreversible or fatal cases of adverse drug reactions from second-line drugs were revealed in some patients. As such 7 (7.7%) developed permanent loss of hearing from the adverse drug reactions. There was 1 (1%) of patient died by suicide. The cause of the suicide was associated with a clinically presumed psychiatric problem from second-line drugs. This was retrospectively mentioned by the attending physician in the patient's clinical chart.

The other type of adverse drug reactions found among patients was hypokalemia, that is, decreased blood calcium level. The majority of the patients, 13 (14%), who

experienced hypokalemia, developed clinically apparent hypokalemic-tetani. Some of the cases with hypokalemic-tetani were documented in the patients' clinical charts to be fatal, that is, such patients died of this specific adverse drug reaction.

The study showed that, from the total of 91 patients, the treatment regimen was modified or permanently changed for 3.3% (3/91) patients due to adverse drug reactions from second-line drugs.

4.2.2.6.3. Trend of the occurrence of adverse drug reactions in the course of patient treatment for MDR-TB

The trend of the occurrence of second-line drugs related adverse drug-reactions during the course of the MDR-TB treatment was assessed to determine the trend of occurrence of the adverse drug reactions in the course of treatment. As such, the study revealed that the majority of the adverse drug reactions occurred during the initial months of the intensive phase of MDR-TB treatment. Except for few adverse drug reactions like the musculo-skeletal and neurological related adverse drug reactions which continued to occur beyond the intensive phase of the MDR-TB treatment, most of the adverse drug reactions were found to occur during the intensive phase months of patient treatment.

The consecutive data depicted in figure 4.4 below show the trend of occurrence of the common adverse drug reactions in the course of patient treatment. As depicted in the figure, there was a decreasing trend in the occurrence of most of the adverse drug reactions related to the major body organs. The common gastro-intestinal related adverse drug reactions from second-line drugs occurred, on average, during the initial five to six months of the patients' treatment for MDR-TB. As in figure 4.4A, anorexia was common during the first five months of the treatment after which it decreased sharply. Similarly, nausea and vomiting (figure 4.4B), was commonly encountered by patients during the first four to six months of the treatment. Moreover, gastritis and symptoms of peptic ulcer diseases (figure 4.4C), commonly occurred during the first five months after commencing treatment. Common to all of the gastro-intestinal related adverse drug reactions was that they started immediately after commencing the treatment for MDR-TB. Compared to other adverse drug reactions, peripheral

neuropathy started later in the course of the treatment but it continued to occur over a longer period in the course of the patient's' treatment. As in figure 4.4D, peripheral neuropathy was common among patients on treatment until the twelfth month after commencing the treatment for MDR-TB.

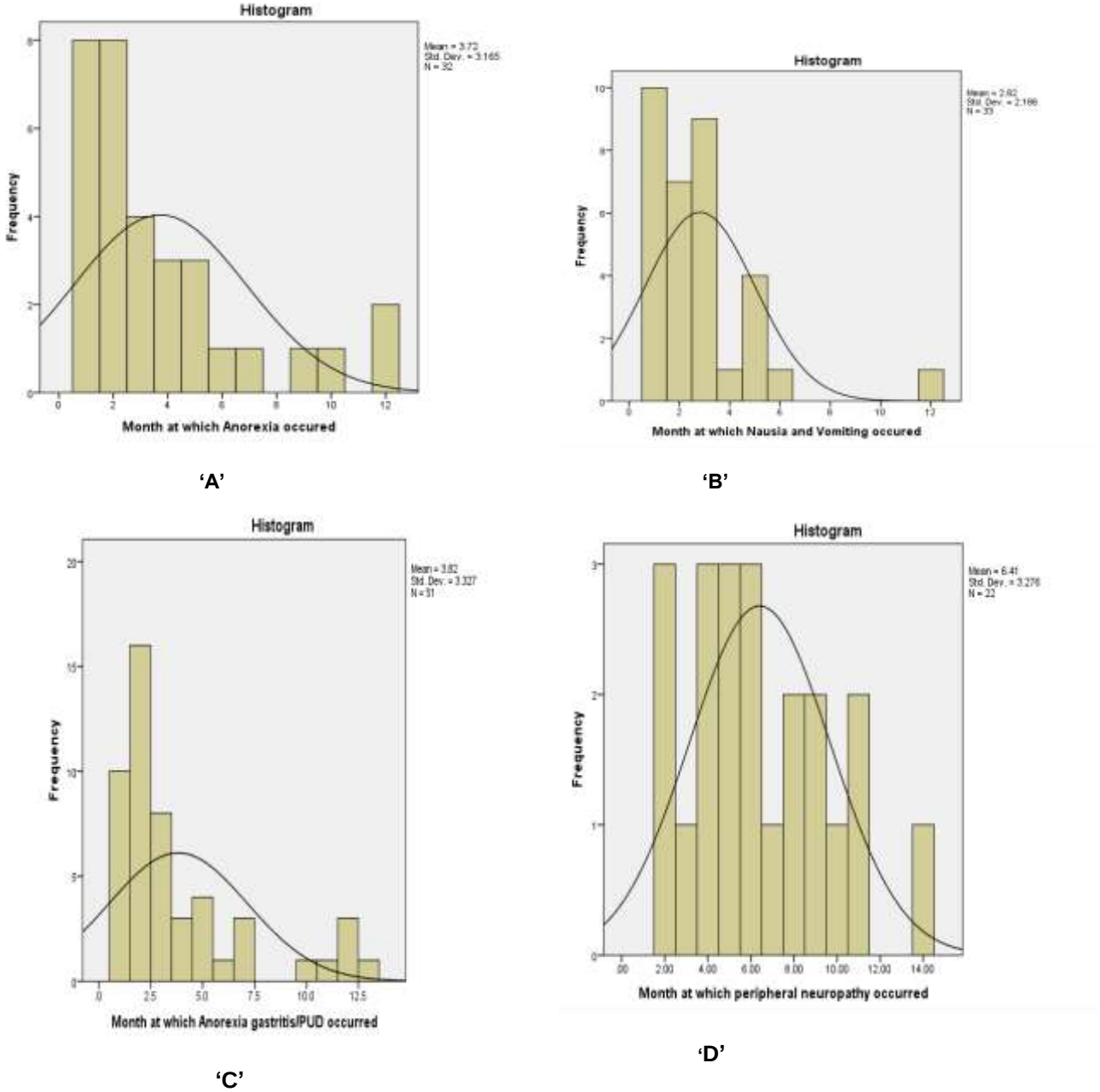


Figure 4. 4: Trend of occurrence of second-line drug related adverse drug reactions by months of MDR- TB treatment among study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=91).

4.2.2.7. Adherence to treatment

4.2.2.7.1. Status of patients' adherence to the daily Directly Observed treatment schedule

From the total of 136 (n=136) patients included in the study, full data on patients' daily directly observable treatment attendance status were available for 93 (n=93) of the patients treated for MDR-TB. The study revealed that, for 100 (74%) of the patients, the daily directly observable treatment service was arranged at the treatment follow up centres as part of the outpatient treatment of MDR-TB. Thirty-six (26%) of the patients with MDR-TB attended their daily directly observable treatment at treatment initiating centres (hospitals).

The assessment of the patient's attendance at the standard daily treatment for MDR-TB through the daily directly observed treatment service, revealed that from total of 93 patients with data, there was strict daily directly observed treatment attendance by 53 (57%) of patients. For the 57% of the patients, there was no evidence of missed daily drug doses. However, for 28 (30%) of patients, the rate of attendance at the daily directly observable treatment, was found to be good but there was evidences of some missed daily drug doses as captured from the patients' chart. Furthermore, for 12 (13%) of the patients, attendance at daily directly observable treatment was found to be irregular with substantial doses of drug doses missed in the course of treatment.

In general, the study revealed that the majority, 81 (87.1%) of the patients included in the study, had an acceptable daily directly observed treatment attendance rate, given the repeated drug toxicities and the associated challenges it posed on patients' adherence.

In this study, all the 91 patients assessed for adverse drug reactions experienced at least one episode of adverse reaction from second-line drugs and also, 41 (31%) of patients had some form of co-morbidity at baseline of which 34 (83%) were due to HIV/AIDS. Given these and the reports of the above scholars, the 87.1% attendance rate at daily directly observed treatment revealed by this study seemed presumably acceptable.

4.2.2.8. Status of laboratory follow up services for patients with MDR-TB in the course of patients' treatment

From the total of the patients included in this study, data on documented routine laboratory follow up service during treatment was obtained for only 39 (n=39) patients. From the 39 patients, 6 (15%) had satisfactory levels of access to routine follow up laboratory services. 33 (85%) had access to follow up services and only very few of the WHO recommended and nationally adopted standard laboratory follow up services. For the rest of the patients with MDR-TB, there were no data found on the patients' clinical follow up chart regarding the follow up laboratory services during treatment. This indicated the absence of standard laboratory follow up services for patients with MDR-TB while on treatment.

4.2.2.9. MDR-TB infection control practices

4.2.2.9.1. Status of tracing the household and the close contacts of patients with MDR-TB

The study revealed that from a total of the patients with MDR-TB that lived with at least one household close contact (n=114), contact tracing was conducted for 60 (53%) of the patients. For the rest of 54 (47%) of patients, it was unknown whether any of their household contacts were traced. The study revealed that, from the total of 136 patients with MDR-TB included in this study, 8 (6%) of the patients were those diagnosed from household contacts of the index patients with MDR-TB. Separate analysis of the eight patients with MDR-TB diagnosed from close contacts revealed that four patients were close contacts of an index case with MDR-TB in one family.

4.2.2.9.2. Coordination of the hospital level MDR-TB infection control practices

It was found that the hospital has a panel team responsible for coordinating the overall programmatic management of drug-resistant TB in the hospital. The hospital MDR-TB panel team, is composed of caregivers from various disciplines including nurses and physicians trained on the clinical and programmatic management of MDR-TB. Moreover, laboratory, pharmacy, environmental health professionals and psychiatrists were also part of the team.

The MDR-TB panel team coordinates the activity of the MDR-TB infection control by the hospitals. The MDR-TB panel team coordinates the implementation of the annual plan on tuberculosis infection control at the premises of the MDR-TB service centres. There is evidence, like archived minutes of discussions held on issues of TB infection control during the scheduled meeting by the hospitals.

It was revealed that supportive staff members were given orientation on the basics of TB infection control at the meetings. At the MDR-TB treatment centre, there were no staff members dedicated for MDR-TB infection control. However, it was reported that the control of MDR-TB infection is the responsibility of all caregivers and persons who are entering into the MDR-TB treatment centre including the patients with MDR-TB.

4.2.2.9.3. Status of the hospital level MDR-TB infection control practices

4.2.2.9.3.1. Adequacy of the inpatient rooms and MDR-TB infection control practices at the inpatient department of the MDR-TB centres

The result of the quantitative checklist used to observe the premises of the MDR-TB treatment centres of the hospitals revealed that the available rooms for patient treated as inpatient at the hospitals have opposite windows. The opposite windows were opened on the day of the observation with signs of good air circulation. The rooms have access to natural light in the morning and in the afternoons. In most inpatient rooms, the average distance between adjacent patient beds was found to comply with the recommendation of the Federal Ministry of Health (FMOH) 2014:143). But it was found that in some cases the distance between adjacent patient beds was less than the national recommendations and that happens during times when higher numbers of patients are admitted to the centre.

There was evidence that patients use plastic container with lids that they used for the collection and disposal of expectorates. The hospital MDR-TB nurse reported that there were adequate N95 masks for use by attending physicians, nurses and those who serve food for patients. It was also observed that patient attendants from family member use N95 mask. It was also reported that the hospital had adequate surgical facemasks for patients.

In general, it was observed that there was evidence of good practice and alertness on tuberculosis infection prevention by all those entering into the premises of the MDR-TB treatment units. The premises of the MDR-TB treatment units were clean but there was no recreation centre dedicated for patients with MDR-TB while they are in the hospitals. As a result, it was reported that there were times when patients with MDR-TB escape through the fences of the hospital MDR-TB centre and inadvertently mingle with the community, which was perceived as a potential risk for MDR-TB transmission to the community.

4.2.2.9.3.2. Hospital practices on isolation of infectious patients with MDR-TB

Caregivers at the treatment initiating hospitals were found to be well aware of the danger of MDR-TB infection. At hospital level, there was evidence of the practice of isolation of infectious patients with MDR-TB. It was revealed that culture converted patients with MDR-TB who are admitted to hospital MDR-TB centres due to any clinical events including adverse drug reactions were kept in separate admission rooms. Newly admitted patients with MDR-TB were kept separately from old cohorts of patients on treatment. Hospital practices in separating culture positive and culture negative patients are in conformity with the recommendations of the Federal Ministry of Health of Ethiopia. Yet all cohorts of patients with MDR-TB share the same lavatory and common recreation area that is dedicated for the MDR-TB centres. Moreover, when many patients share a single room, the distance between adjacent beds in a room were not consistent with the minimum of 1.8 metres distance between adjacent patient beds' that is recommended by the Federal Ministry of Health of Ethiopia.

4.2.2.9.4. Community level MDR-TB infection control practices

4.2.2.9.4.1. Means of patient transport from hospitals to the community level MDR-TB treatment follow up centres

The study revealed that during the initial patient linkage to the community level treatment follow up centres, 97 (92%) of patients were escorted by the nurse caregivers from treatment centres of the hospitals. The hospital ambulances were used to transport patients from the hospitals to treatment follow up centres.

Given that the hospital ambulances were not consistently available to transport all patients with MDR-TB, patients used public transport services to reach the treatment follow up centres and back to their home area as well. Most of the patients linked to the community level MDR-TB treatment follow up centres were not culture converted. As such, the practice of using the conventional public transport service by patients with MDR-TB seemed to be a potential risk factor for MDR-TB transmission to the general community.

Caregivers from both the study sites mentioned that the hospital ambulance vehicles were primarily dedicated for transporting emergency medical cases especially maternal medical emergencies. Thus it was only when the ambulance was freely available that the ambulance was used to transport patients with MDR-TB. Caregivers also mentioned that whenever the ambulance service was used to transport patients to treatment follow up centres, it was used to transport newly diagnosed patients from peripheral health facilities to hospitals. That is, the ambulance was used to transport newly diagnosed patients who were transported to the hospitals for initiation of treatment for MDR-TB.

Once patients with MDR-TB were initiated on second-line drugs, they consistently used public transport to return to the nearby treatment follow up centres. Thereafter, patients use the conventional public transport during their monthly travels to attend the monthly MDR-TB clinic at the hospitals and back to their respective treatment follow up centres and their homes.

4.2.2.9.4.2. Household level MDR-TB infection control practices

Analysis of the status of MDR-TB infection control was conducted for 105 (77%) patients with MDR-TB (n=105) for whom data on household level MDR-TB infection control was available. There was no housing arrangement prepared before the patient with MDR-TB was linked back to the community. There were no MDR-TB infection control arrangements at the patient's household level as well. The result of this study revealed that, 8 (6%) of the total patients with MDR-TB included in this study were diagnosed among household contacts.

Caregivers found at the hospitals and the treatment follow up centres were not implementing the activities recommended on household level MDR-TB infection prevention and control recommended by the Ethiopian National Programmatic Management of Drug-resistant tuberculosis (PMDT) guidelines. Caregivers were expected to ensure minimum MDR-TB infection control practices at the patient's household level for patients linked to community level MDR-TB treatment and follow up services. Yet, this study revealed that caregivers at the treatment follow up centres were not visiting the home area of a patient linked to the community. Thus, the following core activities on MDR-TB infection prevention and control at the patient's household level were not implemented including:

- Collecting information on the number of living quarters available in the patient's home and on the number of household members.
- Educating the family on the support expected from patient's family to enable the patient with MDR-TB to properly adhere to MDR-TB treatment.
- Inspecting the patients' living quarters to make sure that it can address the requirements of respiratory MDR-TB infection prevention at household level
- Ensure that each family member can follow the minimum tuberculosis infection control precautions.
- Making sure that the household level family members who are caretakers of the patient with MDR-TB use respirators as a personal protective measure against MDR-TB infection.

In this way, in view of the MDR-TB infection control recommendations of the national programmatic management of drug-resistant tuberculosis in Ethiopia, the study revealed that there was no practical attempt made by the system on mitigating the problem of MDR-TB infection control at the patient's household level.

In a nutshell, the study revealed that the current practice in the study areas failed to comply with the minimum community level MDR-TB infection control practice recommended by the national programmatic management of drug-resistant tuberculosis (PMDT) of Ethiopia.

4.2.2.10. Decentralization of the MDR-TB treatment services to the community

It was found that patients with MDR-TB were initiated on treatment for MDR-TB at the hospitals. Once they were stabilized, patients are linked to the community level treatment follow up centres, which are health centres.

The study has shown that from a total of 136 patients included in the study, 100 (73%) were linked to the community level MDR-TB treatment and follow up services. For all the 100 (73%) patients who were linked to the community the responsibility of providing daily observed treatment support for the patients was assigned to caregivers found at the treatment follow up centres. Yet, for most of the patients linked to the community level treatment follow up centres data on the daily directly observed treatment support was not complete.

4.2.2.11. Treatment outcomes of patients with MDR-TB at Adama and Nekemte referral hospitals

4.2.2.11.1. Interim (six month) treatment outcome of patients with MDR-TB

For all patients with MDR-TB those enrolled to the treatment for MDR-TB, treatment outcome is evaluated at two phases. These are the interim treatment outcome which is determined at six-month after commencing the treatment for MDR-TB. The other treatment outcome is called the final treatment outcome which is determined at the completion of the treatment for MDR-TB. As shown in the table 4.3 below, analysis of the interim treatment outcome of patients by month six showed that from the total of 136 patients, 97(71%) were culture negative. Twenty-seven (20%) of the patients died by month six. However, the six-month treatment outcome was not evaluated and documented for 12 (9%) patients.

Table 4. 3: Interim (six month) treatment outcome of patients with MDR-TB among study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=136)

Interim (six month) treatment outcome (N=136)	Number (%)
Culture Negative	97 (71%)
Culture positive	0 (0%)
Died by six month	27 (20%)
Six month treatment outcome not evaluated	12 (9%)
Culture Positive	0 (0%)
LTFU	0 (0%)

4.2.2.11.2. Final treatment outcome of patients with MDR-TB

As shown in table 4.4, from the total of 136 patients included in the study, the final treatment outcomes was determined and was available for 110 (81%) of the patients. Twenty six (19%) of the patients were still active and were on treatment by the time of data collection. From the total of 110 (n=110) patients for whom treatment outcome was assigned at time of data collection, 76 (69%) had successfully completed their treatment. From those who successfully completed treatment for MDR-TB, 65 (59%) patients were those who were declared cured. The remaining 11 (10%) patients did not have documented laboratory follow up results but had successfully completed their treatment for MDR-TB. Thus the composite treatment success rate for patients included in this study was 69%. Death was the second higher treatment outcome for patients with MDR-TB included in this study. As such, 30 (27%) of the patients with MDR-TB died from the disease by the twenty-forth months after commencing the treatment for MDR-TB. The treatment outcome of 3 (3%) patients with MDR-TB were not evaluated mainly due to transfers of patients to other treatment follow up centres and reports on their treatment outcomes were not returned to the treatment initiating centres. One patient (1%) was lost to follow ups and the patient was not retrieved until the time of data collection. The details of the patients' final treatment outcomes are shown in table 4.4 below.

Table 4. 4: Final treatment outcome of patients with MDR-TB among study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=110).

1. Final treatment outcome assigned (n=110)	Number (%)
—Cured	65 (59)
—Treatment completed	11 (10)
—Composite treatment success rate (cured & treatment completed)	76 (69)
—Died	30 (27)
—LTFU	1 (1)
—Not evaluated	3 (3)
2. Active and on treatment	26 (19)

Final treatment outcomes of patients with MDR-TB was disaggregated by the hospitals to show differences in the final treatment outcomes of patients by the site of treatment. As shown in tables 4.5 and 4.6, the treatment outcomes of patients with MDR-TB differed by the site of treatment. The 72% treatment success rate among patients treated at Nekemte Referral Hospital was much higher than the 44% treatment success rate among patients treated at the Adama Hospital Medical College. Moreover, there was higher proportion of death among patients treated at the Adama Hospital Medical College (29%) compared to the proportion of death among patients treated at the Nekemte Referral Hospital (12%). The details of the final treatment outcomes by site of treatment are shown in tables 4.5 and 4.6 below.

Table 4. 5: Final treatment outcome of patients with MDR-TB among study participants at Adama Hospital Medical College, Oromia, Ethiopia, December, 2012-September, 2016 (n=79).

1. Final treatment outcome assigned (n=79)	Number (%)
—Cured	32 (40.5)
—Treatment completed	3 (4)
—Composite treatment success rate (cured & treatment completed)	35 (44)
—Died	23 (29)
—LTFU	1 (1)
—Not evaluated	2 (2.5)
2. Active and on treatment	18 (23)

Table 4. 6: Final treatment outcome of patients with MDR-TB among study participants at Nekemte Referral Hospital, Oromia, Ethiopia, December, 2012-September, 2016 (n=57).

1. Final treatment outcome assigned (n=57)	Number (%)
—Cured	33 (58)
—Treatment completed	8 (14)
—Composite treatment success rate (cured & treatment completed)	41 (72)
—Died	7 (12)
—LTFU	0 (0)
—Not evaluated	1 (2)
2. Active and on treatment	8 (14)

4.2.2.11.3. Factors determining the treatment outcomes of patients with MDR-TB

Both bivariate and multivariable logistic regression analyses were used to test the null hypothesis of no relationship between the treatment outcomes of patients with MDR-TB and the patients' socio-demographic and clinical characteristics(Gaur & Gaur 2009:92-98; Healey 2009:293). Table 4.7 shows the status of the treatment outcomes of patients with MDR-TB (n=110) regarding various clinical characteristics of the patients included in the study.

Table 4. 7: Summary of MDR-TB treatment outcome by various clinical characteristics of the study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=110).

Variable	Category	Favourable treatment outcome (cured or treatment completed) (n/%)	Unfavourable treatment outcome (Death) (n/%)	Total (n/%)
Sex	Male	50 (77)	15 (23)	65 (59)
	Female	26 (58)	19 (42)	45 (41)
BMI	<18.5Kg/m^2	40 (60)	26 (39)	66 (60)
	>/=18.5Kg/m^2	36 (82)	8 (18)	44 (40)
Any co-Morbidity at baseline	Yes	18 (53)	16 (47)	34 (31)
	No	58 (76)	18 (24)	76 (69)
HIV	Positive	14 (52)	13 (48)	27 (25)
	Negative	62 (75)	21 (25)	83 (75)
Smear Status	Smear Positive	61 (75)	20 (25)	81 (74)
	Smear Negative	15 (52)	14 (48)	29 (26)
Resistance type	RR-TB	39 (61)	25 (39)	64 (58)
	MDR-TB	37 (80)	9 (20)	46 (42)
Initial Bacillary load	Moderate to high	50 (68)	23 (32)	73 (66)
	No AFB to scanty	26 (73)	11(30)	37 (34)

4.2.2.11.4. Bivariable analyses of the factors determining the treatment outcomes of patients with MDR-TB

At the bi-variable analysis level, the relationship between the dependent variable and each of the predicator variables of interest was explored. This is shown in table 4.8.

Table 4. 8: Summary of bivariate analyses on the determinants of MDR-TB treatment outcomes of the study participants at Adama and Nekemte Referral Hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=110).

Variable	Category	Favourable treatment outcome (cured or treatment completed) (n/%)	Unfavourable treatment outcome (Death) (n/%)	Total (n/%)	Crude OR	Wald x^2 test result	P-value	95% CI
Sex	Male	50 (77)	15 (23)	65 (59)	____	_____	____	_____
	Female	26 (58)	19 (42)	45 (41)	2.436	4.459	<0.035	1.066-5.566
BMI	>18.5Kg/m^2	36 (82)	8 (18)	44 (40)	____	_____	____	_____
	</=18.5Kg/ m^2	40 (60)	26 (39)	66 (60)	2.925	5.327	<0.021	1.176-7.277
Any co-Morbidity at baseline	No	58 (76)	18 (24)	76 (69)	____	_____	____	_____
	Yes	18 (53)	16 (47)	34 (31)	2.864	5.802	<0.016	1.217-6.743
HIV	Negative	62 (75)	21 (25)	83 (75)	____	_____	____	_____
	Positive	14 (52)	13 (48)	27 (25)	2.741	4.795	<0.029	1.112-6.761
Resistance type	RR-TB	39 (61)	25 (39)	64 (58)	____	_____	____	_____
	MDR-TB	37 (80)	9 (20)	46 (42)	2.635	4.608	<0.032	1.088-6.384

From the total of 65 (100%) patients who were cured from the MDR-TB disease, 43 (66.2%) were male while 22 (34%) were female patients. Of the total of 30 (100%) deaths that occurred among all patients with MDR-TB included in the study, 19 (42%) were female patients and 15 (23%) were male patients.

As shown in table 4.8, the study revealed a relationship between the sex of the patients and the treatment outcomes of the patients with MDR-TB. Compared to the male patients with MDR-TB, a higher proportion of death and a lower proportion of favourable treatment outcomes were observed among female patients with MDR-TB (Crude OR=2.436; X^2 =4.459; P<0.035; 95%CI=1.066-5.566).

The study also revealed a relationship between some co-morbidity with MDR-TB at the baseline and the treatment outcomes of patients with MDR-TB. The odds of death from MDR-TB among patients with MDR-TB who had some co-morbidity with MDR-TB at the baseline was higher than the odds of death among patients without any co-morbidity with MDR-TB at the baseline (Crude OR=2.864; X^2 =5.802; P<0.016; 95%CI=1.217-6.743), (See table 4.8).

Moreover, a separate analysis of the patients' cure rate by patients' HIV sero-status revealed that the treatment outcomes of patients differed by the status of MDR-TB co-infection with HIV. Compared to HIV and MDR-TB co-infected patients, a higher cure rate was observed among HIV negative patients with MDR-TB. From the total of 65 (100%) patients who were cured from the MDR-TB disease, 52 (80%) of the cured patients were HIV-negative. HIV co-infected patients with MDR-TB constituted only 13 (20%) of the total patients cured from the disease. A separate analysis of the risk of death between patients with MDR-TB and those patients with MDR-TB co-infected with HIV/AIDS revealed that compared with patients without co-infection with HIV/AIDS, a higher risk of death was observed among patients with MDR-TB co-infected with HIV/AIDS (Crude OR=2.741; X^2 =4.795; P<0.029; 95%CI=1.112-6.761), (See table 4.8)

The study also revealed a relationship between death and patients' body mass index (BMI). As such, the study revealed that the odds of death among patients with low body mass index , that is, BMI <18.5Kg/m2 was about 3 times higher than the odds of death among patients with body mass index greater than or equal to 18.5Kg/m2 (Crude OR=2.925; X^2 =5.327; P<0.021; 95%CI=1.176-7.277), (See table 4.8).

Likewise, the study revealed a relationship between the type of drug resistance and the treatment outcomes of patients with MDR-TB. Compared to patients diagnosed as rifampicin resistant tuberculosis (RR-TB), the odds of death from MDR-TB was higher among patients diagnosed as MDR-TB (Crude OR=2.635; X^2 =4.608; P<0.032; 95%CI=1.088-6.384) (See table 4.8)

Furthermore, at the bivariate analyses level, the study showed an association between the presence of fibrotic (extensive) lung lesion and the treatment outcomes of patients with MDR-TB. As shown in table 4.9, the presence of a fibrotic cavitary lung disease at diagnosis, which is indicative of advanced disease status, was found to have a significant relationship with MDR-TB treatment outcome. From the total of four patients with MDR-TB who had fibrotic lung disease at diagnosis, three patients died of the disease (Phi X^2 =0.405, P<0.017).

Table 4. 9: MDR-TB treatment outcome by presence of fibrotic lung lesion at diagnosis of the study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016 (n=35).

Variable	Category	Death (n/%)	No death (n/%)	Total	Phi X^2 test result	P-Value
Fibrotic Lung Lesion	Fibrotic lung lesion exists	3	1	4	0.405	0.017
	No fibrotic lung lesion	25	6	31		

4.2.2.11.5. Multivariable logistic regression of the factors determining the treatment outcomes of patients with MDR-TB

The determinants of the treatment outcomes of patients with MDR-TB treated for MDR-TB at the two study sites is presented in table 4.8. Regression analysis was used to determine which of the socio-demographic and clinical characteristics best explain variations in the treatment outcomes of patients with MDR-TB (Clark &Creswell 2015:31). Logistic regression model was used to determine independent predictors of the treatment outcomes of patients with MDR-TB. Logistic regression model can fairly be visualised with small number of predictor variables, even though it can be used with up to ten or more predictor variables (Field 2009:211).

Predictor variables with p-values of less than 0.25 are cited in the literature as established factors determining the treatment outcomes of patients with MDR-TB. As such, predictor variables of interest (patients' socio-demographic and clinical characteristics) those with p-values of less than 0.25, that is, predictor variables those effectively predicting the treatment outcomes of patients with MDR-TB were fitted into the final logistic regression model.

For the final multivariable logistic regression analyses, all the assumptions of analyses were checked and were appropriate for the statistical tests used. These included, the normality of continuous variables and multicollinearity effect between independent factors. Moreover, an analysis of the model fit showed that there was no difference between the observed and expected sample values (Hosmer and Lemeshow Test showing P value of 0.757).

4.2.2.11.6. Results of the multivariable logistic regression of factors determining the treatment outcomes of patients with MDR-TB

As shown in table 4.10, the final multivariable logistic regression analyses revealed that the odds of death among patients with MDR-TB who had some co-morbidity with MDR-TB at the baseline was significantly higher than the odds of death among those patients with MDR-TB who were without any co-morbidity with MDR-TB at the baseline (AOR=4.260, 95%CI: 1.607-11.297; P<0.004).

Moreover, the odds of death from MDR-TB among patients with low body mass index (MBI), that is, BMI < 18.5kg/m2 was found to be 2.7 times higher than the odds of death from MDR-TB among patients with body mass index greater than or equal to 18.5Kg/m2 (AOR=2.734, 95%CI: 1.01-7.395; P<0.048).

Furthermore, the odds of death from MDR-TB among female patients with MDR-TB was significantly higher than the odds of death among male patients with MDR-TB (AOR=2.511, 95%CI: 1.005-6.272; P<0.049).

In summary, about 26% of the total deaths from MDR-TB revealed in this study were explained by the three final independent determinants of the treatment outcomes of patients with MDR-TB. These were the presence of some co-morbidity with MDR-TB at the baseline, low body mass index (BMI) (that is, BMI <18.5kg/m2) and being a female patient with MDR-TB (Nagelkerke R Square=0.257).

Table 4. 10: Results of the multivariable analysis using logistic regression on factors associated with unfavourable MDR-TB treatment outcome of the study participants at Adama and Nekemte referral hospitals, Oromia, Ethiopia, December, 2012-September

Variable	Crude OR*	95% CI	P-Value	AOR**	95% CI	P-Value
Presence of any co-morbidity at the baseline	2.864	1.217-6.743	0.016	4.260	1.607-11.297	0.004
Body Mass Index (BMI)	2.925	1.176-7.277	0.021	2.734	1.01-7.395	0.048
Sex	2.436	1.066-5.566	0.035	2.511	1.005-6.272	0.049
HIV	2.7.41	1.112-6.761	0.029	0.088	_	0.767
Drug-resistance type	2.635	1.088-6.384	0.032	2.630	_	0.105

OR* =Odds Ratio; AOR*=Adjusted Odds Ratio

4.3. Results for the qualitative component of the study

4.3.1. Introduction to the qualitative result from the interviews with patients

A total of 18 adult participants, that is, patients with MDR-TB (9 females and 9 males) aged above 18 years was included in the in-depth interviews. Three of the 18 (≈17%) patients openly identified themselves as having some co-morbid conditions with MDR-TB. Two of the 3 patients with MDR-TB were co-infected with HIV while one was a patient with MDR-TB who developed diabetes in the course of the treatment given for MDR-TB.

At the end of each excerpt are initials and a number to indicate the number of the participant and their sex. For example, “P-2M”, with “P-2” indicating participant 2, and “M” indicating the male gender of the participant.

4.3.2. How did the patients with MDR-TB know that they had MDR-TB?

The study revealed that the first trial of tuberculosis diagnosis was made at the nearby health centre for all the patients who participated at the interviews. The first level of tuberculosis diagnosis was made by the use of the basic diagnostic tools including the direct sputum microscopy and the use of radiography.

Many patients with MDR-TB were diagnosed with MDR-TB after the failure of the generic first-line tuberculosis treatment regimen. Indeed, some of the tuberculosis patients reported that the time they spent taking first-line anti-tuberculosis drugs delayed them in the initiation of the second-line anti-tuberculosis drugs given for the MDR-TB. The excerpt taken from one of the patient confirms this:

“…. I completed the six month treatment given for tuberculosis and the cough decreased but did not disappear completely… there was expectoration and cough despite the treatment I was taking…then the nurse told me that I had to start the eight month treatment regimen,… after fifteen days, I submitted sputum and they told me that the type of tuberculosis I suffered from was resistant to the drugs I was taking and I was sent to this hospital,…[P-2M]”.

On the other hand, some of the patients with tuberculosis were promptly diagnosed of MDR-TB after failure of the first six months based tuberculosis treatment regimen. The excerpt below illustrates this.

"…On the same day I completed the six-month treatment, the sputum result was returned,…I completed the six month treatment in the morning and in the afternoon I was called back to the hospital and when I went back, they told me that it is drug-resistant tuberculosis and told me to go to Nazareth, that is Adama hospital…[P-12F]".

Participants mentioned that the larger community does not have insight about the MDR-TB disease and its way of transmission. As such, all the patients included in the in-depth interviews knew that they had MDR-TB only after failure of the generic anti-tuberculosis treatment regimen that they were taking. The below excerpt clarifies low community awareness on MDR-TB:

"…Yea, at our village, people do not know much about MDR-TB. They do not know that the disease is difficult to cure. They do not perceive it as a serious disease…but because now I know about the disease, I refrain from mingling with people… [P-1F]".

The low public awareness of MDR-TB and how transmission occurs may be contributing factors for the higher proportion (6%) of the total 136 patients with MDR-TB who were diagnosed among contacts of the index patients with MDR-TB. The interviews with patients revealed that 2 (11%) of the eighteen patients with MDR-TB who participated in the in-depth interviews were those who contracted MDR-TB from index patients within their own family. One of the two patients blamed health caregivers for not informing her about the possibility of the transmission of MDR-TB from person-to-person.

"…I caught the disease while I was taking care of my husband... the health centre did not tell us that it can be transmitted … [P-6F]".

4.3.3. Patients' perceived quality of the clinical care and services provided for MDR-TB at the Adama and Nekemte Referral Hospitals

4.3.3.1. Level of patients'engagement in the MDR-TB treatment and services related decision making

The main theme from responses forwarded by all participants interviewed, revolved around the counselling and adherence preparation provided by the caregivers for MDR-TB at treatment initiating centres.

The majority of the participants reported that they had discussions with their caregivers regarding the treatment they take for MDR-TB. The main issues of discussions between patients and their caregivers included MDR-TB treatment, the drugs taken and the duration of the treatment. The majority of participants mentioned that they were told what to do in case they encountered unexpected problems during the course of the treatment given for MDR-TB. Thus, the main theme of the reported discussions between patients and their caregivers revolved purely around the medical treatment and services that the patients were getting from clinical caregivers. Patients mentioned that they were not part of the decision made regarding the non-medical services including nutrition for patients with MDR-TB and the financial support they got from the hospitals. The next excerpt clarifies absence of the use of patients' views in nutrition related decision making:

"… I mean it is just three months since I started the treatment, the types of services I get are bed accommodation and food… there is a problem on this issue. I am not given the food that I need, that is good for persons like me who is treated for MDR-TB. We eat the same type of food every day and the same is true throughout the week… we always complain but there are no changes in the type of food we eat….[P-3M].

In this way, it was revealed that the hospitals were not using the views and opinions of the patients with MDR-TB in the planning and implementation of the socioeconomic support provided for patients in the form of nutrition and financial reimbursement. Thus, interviews participants reported that the socio-economic support could not address the needs and preferences of patients with MDRTB.

4.3.3.2. Patients' perception on the responsiveness of the care given for MDR-TB

Discussions were held with patients regarding the caregivers' prompt availability when demanded by patients with MDR-TB. As such, the majority of patients with MDR-TB mentioned that caregivers were not promptly available to the care demand of the patients with MDR-TB. The case was reported to be serious when caregivers were not available in the case of emergent medical events that patients with MDR-TB encountered. A patients who went into comatose status due to absence of prompt care, nervously explained the traumatic experience.

"… at one time I was seriously ill and I was brought by car to this centre. When we arrived, there was no doctor. Then, I fainted and was near death. He came five hours after he was called and that was when I lost consciousness, at that time it means that I was dead…it would have been good if the doctor was here and I was treated on time and I could tell him about the pains and problems I had,…"[P-1F].

Most of the patients with MDR-TB were too weak to help themselves cope with routine personal care they needed. When such patients encountered clinical emergencies that worsened their physical strength, they faced difficult challenges to survive the disease and its treatment. A participant narrated how the absence of prompt clinical care has made patients suffer to the point that they could not cope up with the disease and its treatment.

"…now I am getting stronger, I don't have a problem but for other patients who are weak, it is serious that the caregivers are not available here the whole day, they do not attend to the patients when needed and they only come after the patient enters into coma. I have seen that the situations are endangering many patients in this centre… [P-3M]".

An excerpt of another participant further illustrates the absence of health caregivers:

"…To tell you the truth, in this compound, this nurse is the only one sister who prudently accomplishes her duty. She is good and when she is on duty, she spends the whole night in this compound but we do not get to see the others…[P-5F]".

The majority of patient participants reported that at the MDR-TB treatment initiating centres (hospitals), the communication between caregivers and the patients with MDR-TB was good. Yet, patient participants consistently mentioned that, at the hospitals, the caregivers for MDR-TB were not accessible during emergent disease conditions that patients with MDR-TB face. The excerpt below illustrates how a patient with MDR-TB who encountered an emergent medical condition experienced lack of prompt clinical care for the emergent medical condition that she experienced:

"…we pass a day with our pain and even if we die we die alone… [P-5F]".

Patient participants reported that the difficulty in accessing a doctor for emergent medical conditions is even worse during out of the normal working hours.

"…it is challenging overnight, they only come through if there is a telephone call alerting them…[P-9M]".

If the patient-caregiver communication was good, the complaints that patients with MDR-TB raised would be associated with the lack of full-time physicians who are dedicated exclusively for taking care of the patients with MDR-TB. The interviews with physicians revealed that taking care of the patients with MDR-TB is only one of the many clinical care duties that the physicians are assigned to perform in their hospital.

4.3.3.3. Patients' perception on the status of communication between patients and the caregivers for MDR-TB

Participants invariably mentioned that they were very friendly with caregivers at the treatment initiating hospitals. Some participants reported that the relationship they have with their caregivers at hospitals, surpasses the normal patient-caregiver relationship. It was reported that caregivers at hospitals see patients with MDR-TB as members of their own families.

"….the doctor has been suffering with me and he pays for my transport from his own pocket and also gives me money for my lunch… [P-8F]".

From the interviews with caregivers for MDR-TB, it was revealed that clinical caregivers were involved in non-clinical services provided by the hospital for the patients with MDR-TB. The next excerpt from interviews with a physician illustrates this;

"…in many instances, we personally prepare the breakdown of the financial and nutrition services provided for patients and we submit it to the finance department…in many cases, they are nurses who handle the monthly payments made for patients… we have debates around the budget with them…[P-5F]".

On the other hand, a few participants reported that the way caregivers found at the treatment follow up centres treated them was discouraging. Patients mentioned that they were stigmatized by the caregivers of the treatment follow up centres. The excerpt below illustrates the level of communication between patients and their caregivers at the treatment follow up centres:

"…But the attendance and the care given here at this hospital is very different from the care given at other treatment follow up centres; the care at the health centre is very weak. There are times when caregivers close their doors against us and abandon us and these are educated professionals. There are times when they deny us treatment

for two to three days and we end up phoning the hospital to complain about the situation. …[P-5F].

4.3.4. Patients' perceptions and experiences on the status of the nutrition support available for patients with MDR-TB

A qualitative inquiry was made into the perception of participants on the status of the nutrition support that was provided to patients with MDR-TB by the hospitals. Participants reported that an Ethiopian cultural food called 'injera' with Ethiopian cultural sauce called 'shiro' was the most commonly served food type for patients with MDR-TB admitted at the hospitals.

'Injera' is the most readily available and commonly served staple food in Ethiopia. 'Injera' is a type of bread prepared from a local grain called 'teff'. 'Shiro' sauce is prepared from peas. Participants also mentioned that patients were served with a meat sauce. However, the meat sauce was served to patients irregularly and was of poor quality. They called it a 'watery sauce'.

Participants reported that patients at the outpatient phase of the MDR-TB treatment, got nutrition and transport support during their monthly hospital visits to attend the monthly MDR-TB Clinic Days. The food items that participants received on a monthly basis at the outpatient phase of their treatment included edible oil, lentils, milk powder and grain flour. Both outpatients and inpatients treated at hospitals described the quality and the quantity of the food items that they were getting as poor. Almost all participants were nervous when the issue of nutrition support they get from the hospital was presented for discussion. The excerpts below clarifies this:

"…about the food, it is better not to discuss it [P-9M]; "…we are hurt… every morning, at lunch-time and at dinner, you are given 'injera' with 'shiro' sauce and that is all… [P-1F].

Participants were dissatisfied with the food they were served or given, stating that it is far from being adequate for patients with MDR-TB. An excerpt taken from a participant who was in the outpatient phase of his treatment illustrates this:

"…the food given by the hospital cannot be enough for one month,…not enough unless there is support from parents and relatives …[P-2M]"

Another participants echoed the issue of inadequacy of food for patients:

; "…no, it is not sufficient, how can 10 kilogramme of grain flour be sufficient for one month? It is certainly not adequate [P-8F]".

Sometimes we miss some of the daily meals like breakfast…they say 'we do not have this and that....', how can we take these drugs without having our breakfast?…if we have some money, we go out and eat some 'shiro' and then take the drugs….such problems exist… and in terms of food, we better not talk…[P-9M]".

The second issue most frequently reported by participants was associated with the quality of the nutrition support provided for patients with MDR-TB. Participants reported that the food they were served was tasteless. This means that, participants asserted, patients who had a poor appetite could not eat.

"….even a healthy persons cannot eat the food they give…previously, they used to give us milk, but this time they are not giving us the milk and the drugs are burning me up and how can I digest the drugs that burn me inside? …[P-10M]".

Some participants reported that the MDR-TB disease decreases the appetite of patients and the poor quality of food that they were served at hospital further puts them in a difficult position and they cannot take the treatment on a daily basis.

"…until three months ago, I was only eating fried peas and because I could not eat the food I was served at the hospital… [P-4M]".

The poor quality of the food served at the hospitals was further explained by another participant as illustrated in the excerpt below:

"…when they serve us meat sauce, it is just watery…we could not eat that…it is tasteless, they do not have the ethics…there is a serious problem with regard to the food...[P-5F]".

It was apparent that some participants did not want to engage in discussions releted to the state of the food served in the hospital. But when probed, they narrated their experiences.

"'They served the same type of food every day and it has no taste…sometimes delicious food is needed…important food like eggs are not served'…[P-12F]".

It was also revealed that participants lacked the financial capacity to supplement the food they were given by the hospitals. Many participants reported that they live in rental houses and live on an income that they used to get from daily wage from labour work. It was mentioned that most of the patients were enrolled to the treatment for MDR-TB after a long journey and after at least one course of treatment with first-line anti-tuberculosis drugs. Participants reported that by the time patients were admitted for MDR-TB treatment, they had spent much of what they had for their livelihood. Ultimately, participants highlighted, the MDR-TB disease and the second-line drugs given for the treatment of MDR-TB weakened them. From the participants' point of view, this meant that most patients would not have the strength to continue doing labour work. In a nutshell, the participants noted that patients were not happy both with the quantity and the quality of the nutrition support that they were given by the hospitals.

4.3.4.1. Patients' perception and experience on the status of financial support available for patients with MDR-TB

The qualitative data revealed that patients with MDR-TB were reimbursed for the transport costs that they had incurred. Patients went to hospitals on a monthly basis to attend their monthly clinical follow up services and also to collect the nutrition support that they were given by the hospitals.

Participants reported gaps in the financial support that patients with MDR-TB received from hospitals. Firstly, they noted that hospitals reimbursed transport costs if the patients produced official receipts. Participants also mentioned that patients could only obtain transport receipts from vehicles that travel long distances and had not obtained receipts from local transporters like taxies and carts even though they had made payments during their monthly travel to and from the main bus stations. This meant that, participants emphasised, transport costs for taxies and carts remained unnoticed and were not refunded. Secondly, participants noted that during the long outpatient phase of their treatment, patients pay transport costs for transporting the food items that they were given on a monthly basis. They highlighted that the cost of transporting the food items, from the hospitals to their home, was not considered in the financial support that they get from the hospitals. Thirdly, patients and caregivers equally reported that there were times when patients were given less financial support than the amount they needed for their monthly visits to the hospitals. The next excerpt from a caregiver illustrates this:

"… there were incidences when patients were paid for single trip transport costs…….as a result, we had debates on budget; they said that the budget had been used up, even when the funds were actually available….[P-5F].

4.3.4.2. Patients' perception and experience on the conditions of service-setups at the hospitals

The majority of participants reported that the open compound within the premises of the MDR-TB treatment units in the hospital was clean. Thus, most participants were happy with the cleanness of the compound of the hospital MDR-TB units.

On the other hand, participants narrated that the patients' living rooms and the toilets, including the shower rooms, were not clean. Participants mentioned that the toilets dedicated for patients' use, were not emptied timely. Participants stressed that there were times when the toilets were full and spilt over, making it difficult for patients to use them. In the same way, the living rooms of patients treated as inpatients were not cleaned on a daily basis mainly because of the absence of a dedicated cleaner who could daily clean the toilets, the shower rooms and the living rooms of patients treated as inpatients.

Participants claimed that patients were not allowed to go out of the premises of the MDR-TB treatment unit. Yet, participants noted that there was no recreation quarter dedicated for patients with MDR-TB on the premises of the MDR-TB treatment units. According to participants, it was for this reason that patients were bored of staying in the premises of the hospitals MDR-TB units. The next excerpt taken from a participant treated as inpatient at a hospital clarifies how a social exclusion started at home further worsened by the situation at the hospital MDR-TB treatment units:

"… the social life, you cannot live with others. I know what happened to me…before I came here, all the neighbours and all family members avoided me….when they brought me to this hospital, here also there was no recreation and that affected me mentality until now, they give me food and you can say that it is a prison for me. It is difficult to be separated from family. It is what God gave me and I did not buy the disease… [P-14M]".

4.3.4.3. Level of patients' satisfaction with the overall care and services given for MDR-TB at the Adama and Nekemte Referral Hospitals

A substantial number of participants reported that patients were satisfied with the clinical care that they were getting at the hospitals. They mentioned that, when available, caregivers at the hospitals were respectful and caring towards patients with MDR-TB. They also mentioned that most of the hospital caregivers were approachable to discuss patients' treatment related issues.

"…wow! it is unparalleled, especially the female nurse, I do not know or you may ask all patients but they will tell you the same thing… …she calls us when we are at home and I have two cell phones of her…[P-18F]".

The friendliness of the hospital level caregivers was consistently reported upon by the majority of the participants. They noted that the hospital level caregivers are caring when they are available in the MDR-TB treatment centre. Most participants were thankful for the clinical care they were given at the hospitals.

"…With respect to the treatment given I think it is enough…since I started the treatment, all doctors have been supporting me…today I completed the treatment given for MDR-TB… …I want to thank them all…[P-17M]".

Participants reported that a patient with social problems, stayed at the treatment initiating hospital for the first 8 months of the treatment, until the injection based treatment is completed. A participant who had social problems and who was allowed to stay at the hospital until he completed the injection based treatment narrated that he was happy with the care and services provided by caregivers at the hospital.

"… I stayed here for a long time and it is very good and I want to say God bless… they did not harm me and also I have seen them attending to other patients as well…regarding those who die, it is because their date of death is due, otherwise they are good in treating us…[P-10M]".

Another participant reported similar feelings of happiness expressed by patients about the clinical care and services that they received at the treatment initiating hospitals.

"…I can say that the sister giving me the drugs is my mother… I have the same respect that I have for my mother. I was about to commit suicide because of the drugs but her advise saved me… [P-4M]".

However, there were a few participants who angrily reported that caregivers at the treatment follow up centres mistreated them. They also reported that there were times when the patients were denied routine societal norms of interaction like salutations by some caregivers at the treatment follow up centres. The next excerpt clarifies this:

"…there are times when the caregivers at the treatment follow up centres closed their doors against us and abandoned us…they do this even though they are educated professionals…there are times when we missed drugs for two or three days… we phoned the hospital and complained about the situation…[P-10M]".

4.3.4.4. Patients' perception and experience on the social impact of becoming a patient with MDR-TB

Participants reported a range of social and economic impacts caused by being a patient with drug-resistant tuberculosis. Separation from family members and the feeling of loneliness are the most frequently encountered forms of the social impact of being a patient with MDR-TB. The main reason for separation from immediate friends and family members was reported to be the fear of disease transmission to others.

"…it separated me from people… you do not work because you do not have the strength to work, and also the attitude of people towards the disease is not good…it means living alone, sitting alone and it is just lonely living…[P-1F]".

Participants reported that the public does not have insight on MDR-TB and how it is transmitted. Instead, patients with the disease try to take care of the community around

them, based on the information they obtained from caregivers for MDR-TB. The next excerpt shows this:

"…because people do not know about the disease, they do not consider it to be a serious disease but because I know about the disease, I refrain from them… [P-1F]".

On the other hand, participants noted that when familities and close friends know the dangers of MDR-TB transmission, they tend to avoid patients with the disease. Participants also noted that the way in which caregivers taught families and friends on MDR-TB was not appropriate as it made them frustrate about the disease. As the result, in some instances patients were denied the support they needed from families and close friends.The excerpt below clarifies this:

"……before I came to this hospital, the health workers came to our home and they said that the disease transmits at the distance of one meter,… and all the neighbours, friends and all family members avoided me….[P-14M]."

4.3.4.5. Stigma on patients with MDR-TB

Participants mentioned that the community does not have knowledge of the disease, MDR-TB. On the other hand, when they got to know about the dangers of MDR-TB and the risk of its transmission to family members and neighbours, patients were discriminated against by their own families and their neighbours.

"…you cannot live with other people, I know what happened to me, all the neighbours and all my family avoided me and that hurt me very much mentally. Even now in the hospital I live alone and it is a state of prison for me. It is difficult to be separated from family. It is what God gave me and I did not buy the disease… the disease discriminates patients from their own family, now I look forward to seeing the day when I will sit in the family's saloon again… [P-14M]".

Discrimination was repeatedly talked about by participants. They claimed that there were patients who were discriminated or avoided by their own family members and their friends. Moreover, participants mentioned that patients with MDR-TB were even blamed by own family for developing the disease-MDR-TB.

"…compared to their attitude before the disease, I mean the attitude they have towards me has changed and they say to me 'go away', 'stay there'…I know that it is important to separate utensils and living room but the way they approach me does not show any respect...they say to me 'you brought this disease unto us' 'go away!'…[P-9M]".

Some participants also reported that the way in which caregivers tell the community about MDR-TB makes the community to panic and avoid patients. The participants attributed the discriminatory practices of the community to the incorrect manner in which the families and friends were taught about MDR-TB by the hospital and the health centre level caregivers.

The interviews with the patients also revealed that patients with MDR-TB were also discriminated by caregivers, especially those at the treatment follow up centres. An excerpt from a patient illustrated this:

"…I was a first year university student…I discontinued my education to be treated and cured from this disease but I have discovered that only a few people provide services with respect. Some of them do not even consider us as human…they do not act professionally and sometimes we wait for five to six hours to get the daily medication we need…[P-13M]."

Most participants felt that all human beings who breathe in air are at risk of MDR-TB. Thus, avoiding patients with MDR-TB is not a good practice. An excerpt taken from a participant who experienced stigma due to becoming a patient with MDR-TB clarifies this:

"…This disease is not what someone caters from somewhere else, but it is caused incidentally…when people know that we have this disease, they discriminate us more…[P-9M]."

Pointing to the healthcare givers at the treatment follow up centres, participants were particularily angry while reporting the issue of stigma from the caregivers.

"…as we are victims of the disease we should patiently wait for the drugs but to properly control the disease and to prevent the disease from transmitting to the community the best treatment should be given for us as patients, …,if they abandon us what kind of attitude and response we will have for the community…we should have learnt good things from them. I have been asking about this but there is no any response I get from them,…there was one female nurse who provides us the treatment and if she is not there we have to suffer and we need to go to the directors' office and complain,…even when we enter the health centre compound they run away, and while knowingly that we should be given medication they run away not to give us the drugs…[P-13M]."

In these ways, patients with MDR-TB experienced stigma from family members, close friends, neighbours and the health care givers.

4.3.4.6. Patients' perception and experience on the economic impact of becoming a patient with MDR-TB

15 of the 18 participants of the indepth interviews with patients mentioned that they were not engaged in any income generating work at the time of this data collection. The same participants mentioned that before being diagnosed of MDR-TB, they used to cater for their daily subsistence by engaging in different types of labour work from which they received daily wages. Among the participants, there were two drivers and one soil technician with degree level training. The two drivers and the soil technician were all employed by private companies. All participants reported that they quit their jobs after enrolment to the MDR-TB treatment, maily as the result of enrollement to the treatment for MDR-TB. Stigma on patients with MDR-TB and lack of the physical

strength to continue work were also noted by participants as the cause for the interruption of employment. The next excerpt clarifies this:

"…yes, before I got the disease, I was free to move around and cater for myself. But after I got the disease there was a big problem, people did not welcome me and their attitude became negative towards me and also, I did not have the strength to work like before…[P-2M]".

Some participants reported that termination of employment due to MDR-TB and its treatment has resulted in such patients face difficulty to continue taking care of their family dependents. The next excerpt was narrated by a participant who was weeping while telling his story:

"…I was formally employed… I am a soil laboratory technician and I have a degree in that science… as I was employed by a private company, my income was discontinued since I caught this disease and could not continue the job... I also could not support my family, so that the disease brought big problems in my life. That is it!... [P-3M]".

Some participants also believed that their poor economic status and the poor quality of food that they used to eat have put them at risk of contracting the MDR-TB disease.

"…yes, there is an economic problem and I used to work on daily labour work with the privates,…I eat when I get food and do not eat when I do not have something to eat and because of this, I cought the disease and the disease affected me a lot and I became extremely unwell [P-5F]".

Another participant used a similar phrase to associate poverty with the MDR-TB disease:

"…I think it may be from hunger and thirst that I caught the disease because I was employed in daily labour work and I worked in the deserts where there was no food and water…[P-15M].

As a result, there were some poor patients who considered being a patient with MDR-TB as a sign of bad luck. Because such patients thought that they contracted such a bad disease, the treatment of which is intolerable. An excerpt taken from a patient participant who could not define his life situation makes clear the impact of MDR-TB on the patients' life as follows:

"…I usually asked myself why I had caught this disease and why I took such drugs…[P-3M]".

4.3.4.7. Status of patients' adherence to the MDR-TB treatment and associated factors

The majority of the participants reported that they adhered to the instructions and advises of the caregivers for MDR-TB. Despite the fact that the second-line drugs were difficult to be taken on a daily basis, participants mentioned that they knew about the danger associated with interrupting the treatment given for MDR-TB. These participants also reported various factors that challenge patients' strict adherence to the treatment given for MDR-TB. These factors are illustrated in the sections that follow.

4.3.4.7.1. Perceived seriousness of the disease

The study revealed that some of the patients with MDR-TB were doubtful about the chance of getting cured from the MDR-TB disease. The perceived seriousness of the disease MDR-TB was heart-breaking for some of the patients with the disease. Perceived seriousness of the disease as one of the reasons that made some patients pessimistic while still taking the treatment given for MDR-TB is captured in the next excerpt:

"…the disease is deadly…out of five of us that were admitted at the same time to this hospital, only two of us were discharged alive and the other three patients died of the disease… [P-4M]".

Participants reported that patients' perceived seriousness of the disease was one of the factors detracting patients' commitment to continue treatment. While tolerating the drug related adverse drug reactions from the second-line drugs, some patients still worried about the outcome of their treatment.

"…the treatment is good but there are patients that do not improve at all and do not return home alive…[P-2M]".

It is clear from the above excerpts that the patients' perceived seriousness of the disease, MDR-TB, is one of the clinical service areas needing attention by the caregivers for MDR-TB.

4.3.4.7.2. Adverse drug-reactions from second-line drugs

The study also revealed that adverse drug reactions from second-line drugs were noteworthy factors that put patients in a difficult position in terms of adhering to the standard treatment given for MDR-TB. All of the 18 patients who participated in the interviews with patients had the experience of second-line drugs related adverse reactions while on treatment. Participants reported that the drugs taken for MDR-TB were miserable and it was too difficult for them to take the drugs daily. The next excerpt shows the experience of a patient taking second-line drugs for the treatment of MDR-TB:

"…above all, the drugs are miserable, especially the last two drugs were very dangerous and were not even good for mankind to take. Indeed, they made my blood vessels and my eye to burn up. It was very difficult to take them, I would be happy if those drugs were changed to injections or other drugs. If I took the drugs and drank milk, I vomited; it was as if there was poison in the food I ate and I vomited. I felt as if my body was tied up with a rope and my mind stopped working and even I could not properly see at that time…[P-7F).

The same experience was reported by another participant regarding the challenges that patients face from adverse drug reactions, as in the next excerpt:

"…for at least three hours after taking the drugs, you felt different …especially after taking the two drugs…[P-3M]".

Another participant had the same experience as evidenced in the excerpt below:

"…I took the drugs and immediately went to sleep or else I would not feel good …[P-18F]".

While still continuing the treatment given for MDR-TB, some patients feared picking up another disease due to the adverse drug reactions. For some of the patients, the severity of the adverse drug reactions affected their joints.

"…once I developed the disease I tried to tolerate all the burnings…I usually ate a piece of sugarcane just to sooth my body…I had pain in the joints but the doctor said that it would disappear and I should take it easy but still, it continued and became more severe…[P-10M]".

As such, the above excerpts makes it clear that adverse drug reactions from second-line drugs, is one of the clinical factors challenging patients' adherence to the standard treatment given for MDR-TB.

4.3.5. Perception and practices of caregivers for MDR-TB on the functionality of the programmatic management of MDR-TB

4.3.5.1. Introduction to the qualitative result from the interviews with caregivers for MDR-TB

The qualitative inquiry was also used to explore the perceptions and the practices of caregivers for patients with MDR-TB regarding the functionality of the programmatic management of MDR-TB at the Adama and Nekemete Referral Hospitals. Eleven caregivers for patients with MDR-TB participated in the in-depth interviews with caregivers. The interviews with the caregivers included three male medical doctors and eight nurses (5 female and 3 male) who were active caregivers for patients with MDR-TB at the two study hospitals included in this study. In the same way as for the qualitative report for the patients with MDR-TB, at the end of each excerpt are initials and a number to indicate the number of the participant and their sex. For example, "P-2M" , with "P-2" indicating participant 2, and "M" indicating the male gender of the participant.

4.3.5.2. Caregivers' perception and experience on the adequacy of the nutrition support provided for patients with MDR-TB

The study revealed mixed experiences of caregivers regarding the status of the nutrition and financial support given for patients with MDR-TB. About half of the caregiver experienced that the nutrition support that patients with MDR-TB got from the hospitals while they were treated as inpatients at the hospitals was relatively adequate. However, the same participants mentioned that the nutrition support that patients with MDR-TB got during the outpatient phase of the MDR-TB treatment was virtually inadequate and of poor quality.

"…patients with MDR-TB are very poor…they do not have anything…we give them Plamynut...it is not enough, it is very difficult for poor patients to take the drugs without adequate food,…there are many complaints from patients,…[P-4F]".

Similarly, a participant who was responsible for the care of patients with MDR-TB at a treatment follow up centre narrated that while the drugs and supplies are available for the patients, the problem associated with the nutrition support given for patients was a challenge.

"…from the perispective of distance, from the perispective of finance, nutritionally there is visible problem. But the provision of drugs is very good, there is enough supplies, and there was no incidences of interruption,…[P-2F."

Only a small proportion of caregivers who participated in the interviews reported that the nutrition support and the cost of transport that patients with MDR-TB were given was acceptable.

4.3.5.3. Caregivers' perception and experience on the quality of the nutrition support provided for patients with MDR-TB

The study revealed that the quality of the food items that patients with MDR-TB were given was one aspect of the challenges associated with it. Caregivers reported that the food items that were provided for patients lacked protein and in the meantime, patients with MDR-TB need high protein rich food. An attending physician described the situation in the next excerpt:

"…as a physician treating patients, I do not believe, patients should get a variety of food items and it should be given based on their preferences ,…they are given 10 kilogramme of grain flour per month, 2 packs of pasta and half (½) a kilogramme of milk powder. The majority of the food items are not body building, the food items given currently are sources of more of carbohydrates, how does the grain flour help and those foods given simply because it is food …I do not support much because patients should get variety of food and also based on their interest; I have also seen that patients want to select the type of food that they want to eat,… even for patients with basic TB those treated for six months, we need to give high protein diet. We get those high protein diets from food items like the egg, milk and it can be from other foods like the beans.

But the food items currently given for MDR-TB patients are more of carbohydrates,…it is not like egg, even though milk is available in the form of powder, it is not what patients prefer. Therefore to say that it really builds their body and prevent their body from this disease evev as the science states it should be protein foods like egg and milk,…[P-7M."]

Thus, it is made clear in the above excerpt that patients with MDR-TB need to be provided with body building food items they prefer and like and must satisfy the clinical nutrition needs of each individual patient. For this, participants in the interviews, recommended the need to establish a strong monitoring mechanism from the Regional Health Bureaus to make sure that patients with MDR-TB are actually getting the right nutrition and the full benefit from the package of treatment enabler schemes which they are eligible to.

4.3.5.4. Caregivers' perception and experience on the management of the nutrition and financial support schemes for patients with MDR-TB

It was invariably and desperately reported that the personnel in charge of facilitating the implementation of patient support schemes, at the hospitals, were virtually not cooperative. Therefore, caregivers for MDR-TB reported that on top of the technical healthcare they provide for patients, nurses and physicians were also responsible for facilitating the execution of the monthly patient transport and nutrition support activities.

"…there are times when the finance department does not volunteer to go and make payments for the patients,…they mistreat us saying 'your patients' as if the patients with MDR-TB were our family members,…sometimes they say that the budget is used up even when the funds are actually available. In most cases it is the nurses who handle the payment for patients, nurses also arrange and distribute nutrition items to each patient. The problem is not the absence of money but it is the way it is utilized…[P-8M]."

One of the issues that the study revealed is that patients with MDR-TB are expected to pay towards transporting the food items they were given by the hospitals. Most of the patients were from distant rural areas, using public transport. The impact of the cost that patients incurred to transport food items was mentioned by the majority of the caregivers who participated in the interviews. This cost, as was revealed, was an overlooked cost from the point of view of the programme of MDR-TB but it was important for patients with MDR-TB.

4.3.5.5. Caregivers' perception on level of health system's support to the programme of MDR-TB

Some caregiver participants mentioned that there was positive support from the management of the respective town, provincial and district health management offices. There were also reports that the management of the hospitals and the treatment follow up centres in some facilities were supportive to the programme of MDR-TB. An excerpt taken from one of the participants makes this clearer:

"...the town health office comes and supervises me…I ask questions and they encourage and support me and in my opinion, that is good… [P-1M]".

However, the majority of caregivers bitterly noted that they do not feel supported by the management of the immediate health offices and the management of their own health facilities. This was mentioned in terms of the absence of supportive supervision visits from the immediate district and provincial health offices. Participants added that the management of the immediate health offices did not even make telephone calls to them unless they needed reports in three months' time.

"…regarding the MDR-TB I don't think that the district health office even knows the problem...[P-2F]"

It was mentioned that the immediate technical managers managing the same premises of the health facility, did not emphasise the management of drug-resistant tuberculosis.

Caregivers cited that there were clear incidences whereby individuals and employees working in the same health facility and in the same hospital or health centre, feared approaching the patients with MDR-TB and even entering into the centres where these patients were treated.

"…I think that the managers at a higher level did not focus attention on the programme of MDR-TB and that is why the heads of the health centres did not give priority to the issue of MDR-TB…[P-3M]"

Similarly, some clinical caregivers who were responsible for initiating patients with MDR-TB on the second-line drugs, mentioned that the technical management and those responsible for facilitating the use of the budget allocated for the programme of MDR-TB were not supportive of the programme.

"…a physician who is assigned to the MDR-TB clinic is responsible for everything. If water and electricity are discontinued, it is the physician assigned there who ensures that these needs are provided. We are also logisticians as we take the responsibility of patient transport; we are finance personnel as we are responsible for arranging payments for patients;…this is because they do not support us. We are pharmacists because we receive and dispense drugs for the patients. We are laboratory technologists it is us who collect and send the laboratory samples…around the hospital management there is no question that the support is very poor. It is very poor. We debate repeatedly and have criticized them repeatedly…I have notified the Oromia Region Health Bureau, they do not perceive the issue of MDR-TB as you do…[P-5M]

Participants also mentioned that the number of trained caregivers at the treatment initiating centres was inadequate. It was further indicated that the number of caregivers for MDR-TB who were trained and deployed by the health management system, especially at the treatment follow up centres, was inadequate. The caregivers mentioned that at the MDR-TB treatment follow up centres, there was only one

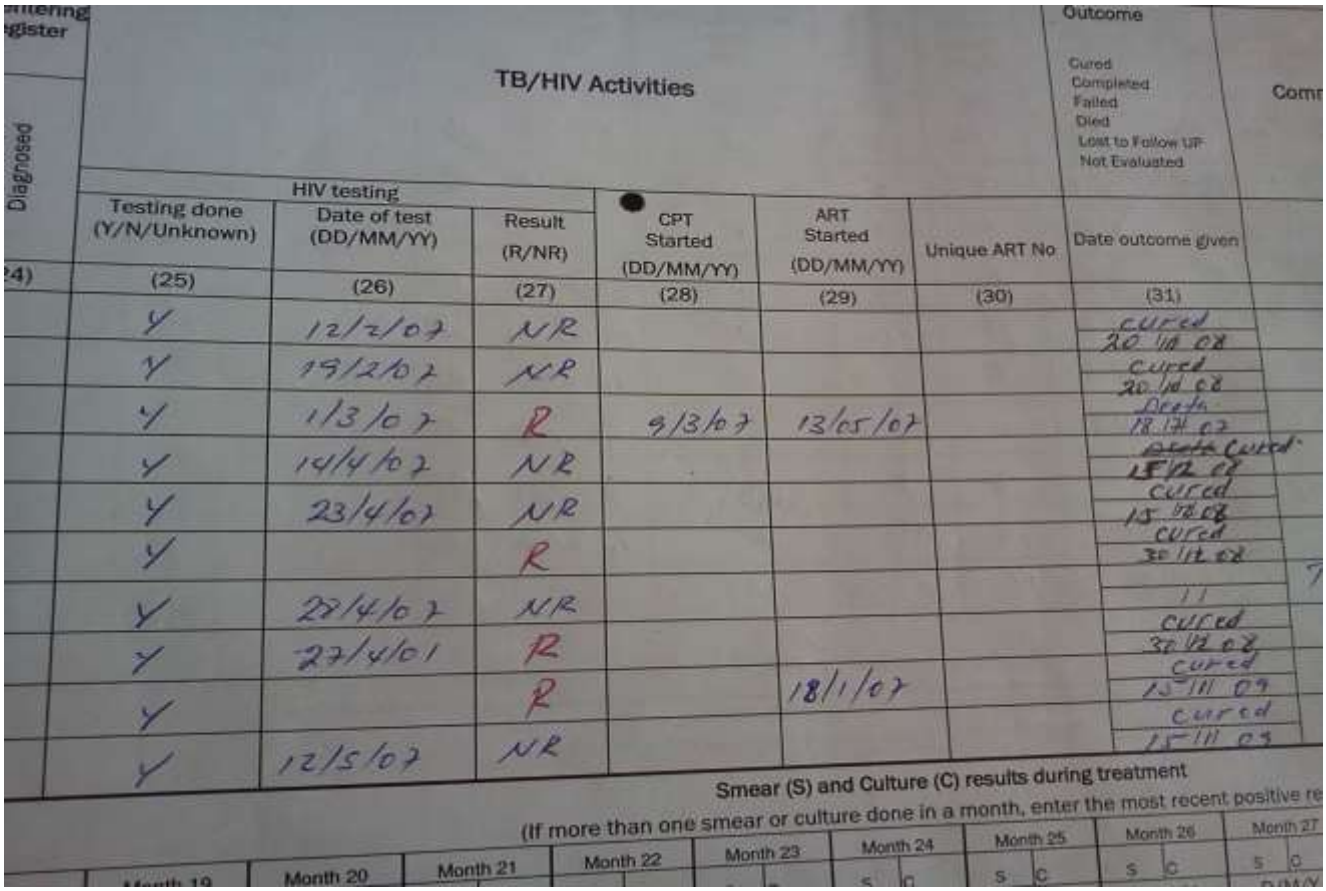
caregiver who was responsible both for the generic programme of tuberculosis and for the programmatic management of drug resistant tuberculosis.

4.3.5.6. Caregivers' experience on management of MDR-TB and HIV/AIDS co-infection

All participants reported that the substantial number of patients with MDR-TB who had enrolled to the treatment of MDR-TB was co-infected with HIV. Caregivers mentioned that the clinical management of patients with MDR-TB who are co-infected with HIV was challenging. Moreover, participants reported that the majority of the deaths from MDR-TB were observed among the HIV co-infected patients.

"…thirty percent to forty percent of the MDR-TB patients who have been receiving treatment had both HIV and MDR-TB. The mortality rate for this co-morbidity is very high and the patients' chance to die is very high…[P-7M]".

The idea of the above excerpt was also supported by what was captured through a photograph taken from the patients' MDR-TB unit register as shown in figure 4.5 below.



Diagnosed	TB/HIV Activities						Outcome	Comm
	HIV testing						Cured Completed Failed Died Lost to Follow UP Not Evaluated	
	Testing done (Y/N/Unknown)	Date of test (DD/MM/YY)	Result (R/NR)	CPT Started (DD/MM/YY)	ART Started (DD/MM/YY)	Unique ART No	Date outcome given	
4)	(25)	(26)	(27)	(28)	(29)	(30)	(31)	
	Y	12/2/07	NR				cured 20/12/08	
	Y	19/2/07	NR				cured 20/12/08	
	Y	1/3/07	R	9/3/07	13/05/07		Death 18/12/07	
	Y	14/4/07	NR				death cured 15/12/08	
	Y	23/4/07	NR				cured 15/12/08	
	Y		R				cured 30/12/08	
	Y	23/4/07	NR				11	
	Y	27/4/01	R				cured 30/12/08	
	Y		R		18/1/07		cured 15/11/09	
	Y	12/5/07	NR				cured 15/11/09	

Smear (S) and Culture (C) results during treatment

(If more than one smear or culture done in a month, enter the most recent positive re

Month 19	Month 20	Month 21	Month 22	Month 23	Month 24	Month 25	Month 26	Month 27
					S C	S C	S C	S C

Figure 4. 5: Status of MDR-TB and HIV co-infection among patients with MDR-TB treated at the two referral hospitals, Oromia, Ethiopia, December, 2012-September, 2016.

Participants reported that the MDR-TB centres were not providing services for HIV. Caregivers for MDR-TB were not trained on HIV care and support services. As caregivers for MDR-TB did not have the training, they were not prescribing anti-retroviral drugs for patients with MDR-TB who were co-infected with HIV. Also, the MDR-TB treatment centres did not have anti-retroviral drugs as the anti-retroviral drugs were not kept in the MDR-TB treatment centres. This problem was found both at the treatment initiating centres and at the treatment follow up centres.

It was revealed that the MDR-TB treatment initiating centres were providing HIV test services for patients enrolled to the treatment for MDR-TB. But they did not have the training and the drug supplies to prescribe anti-retroviral drugs for those patients with MDR-TB whose HIV test result were positive. Thus, all the participants who were caregivers, consistently reported that patients with MDR-TB who were co-infected with

HIV/AIDS were referred to other centres for the treatment and care that they needed for HIV. As such, this patient group suffered a lot of inconveniences in seeking care for both diseases at different centres and from different caregivers.

"…in our hospital, there is a separate centre where services for HIV are given and patients are referred to them but there is no system in place whereby we collaborate and work jointly…this is an area where we have been facing problems…[P-8M].

A similar excerpt was obtained from another participant's narrative:

"…In our setting, the hospital and the MDR-TB centre are not in the same compound,…the patients' main follow up place for the anti-retroviral therapy is a separate clinic so they have to go there…it would have been best and could have improved many things if anti-retroviral therapy were given at the MDR-TB clinic itself…[P-5M]".

A physician participant who was treating MDR-TB and HIV/AIDS co-infected patients, desperately narrated an incident of a sudden death that occurred to an MDR-TB and HIV/AIDS co-infected patient on his 17th month of the treatment given for MDR-TB. The patient was on anti-retroviral treatment for seven years before he was diagnosed of MDR-TB.

The main explanation reported was that co-infected patients focused on the new problem of MDR-TB and the challenges associated with taking both the second-line drugs and the anti-retroviral drugs. After he had enrolled to the treatment for MDR-TB, the patient could not follow the routine follow up services given for patients on treatment for HIV/AIDS. As such, while the patient was hopefully completing his treatment for MDR-TB, he died possibly because of failure of the treatment given for HIV/AIDS. The failure of the anti-retroviral drugs was not diagnosed until the patient was found fell down in the street.

"…The patient was found in the street. The patient had been on anti-retroviral therapy for seven years. Then they brought him in and when I saw him, his T-lymphocyte cell bearing (CD4) count was forty. I believe he died because of anti-retroviral therapy failure. The patient had been on MDR-TB treatment for seventeen months and had converted culture…therefore I believe that if there had been follow up services on HIV at our hospital it would have saved the life of the patient….[P-5M]".

4.3.5.7. Caregivers' experience on the occurrence and the management of adverse drug-reactions from second-line drugs

Participants reported that the majority of patients treated with the second-line anti-tuberculosis drugs experienced various forms of adverse drug reactions.

"…patients said that the drugs burn them up...and also complained that the drugs changed the colour of their urine…the behaviour of patients taking these drugs was also changed…[P-2M]".

In some patients, the adverse drug reactions were challenging both to diagnose and treatment them. Many caregivers desperately talked about the adverse drug reactions that patients with MDR-TB encountered and the challenges of detecting and managing them. The diagnosis of some of the adverse reactions needed laboratory follow ups which were not readily available in the hospital.

"… well, in our hospital, organ function tests are available but others like the thyroid function test and the electrolyte tests are not available, it would have been very good if they were available and were done at the hospital. As a result of these tests not being available, there were problems like the incidence of the sudden death of patients that occurred. I felt the pain as an individual and as a physician who is working there. I hope the situation will improve… [P-7M]".

Moreover, caregivers noted that there were times when they face shortage of the drugs needed to treat adverse drug reactions among patients with MDR-TB.

4.3.5.8. Caregivers' experience on the challenges associated with the adverse drug reactions from second-line drugs

The study revealed that adverse drug reactions caused both social and medical problems on patients who were affected by the problem. The first problem on patients affected by adverse drug reactions was social in terms of misunderstandings by the patients' family and close friends. This was expressed by the majority of the participants. For example, the incidence of drug induced psychological problems created misunderstanding between patients with MDR-TB and their families. There were patients with psychological derangement caused by adverse drugs reactions and who were seen to disagree both with their families and their health caregivers. A nurse caregiver narrated an incident whereby a psychiatric problem arising from second-line drugs in a female patient with MDR-TB resulted in a misunderstanding with her family members.

"…she was living with her mother and father, but when I went there, she had nothing to eat. She had brothers but they could not understand her. I had also talked to her brothers about the prevailing situation. At that time, she was also psychologically disturbed. It was observed that these drugs have a psychological effect on patients. Patients taking these drugs usually change their behaviour, they are not their usual selves. Her brothers had a different perception about her behaviour…[P-3M].

From the above excerpt, it is clear that family members of the patients did not understand the causes of the changes in the patient's behaviour. The majority of the caregivers for MDR-TB knew that patients with MDR-TB who are initiated with second-line drugs face challenges associated with adverse drug reactions. Some caregivers reported incidences whereby patients with MDR-TB developed permanent loss of hearing. There were also patients who developed depression, as was noted, among which there was one case of suicide. Caregivers also mentioned that a substantial number of patients with MDR-TB were repeatedly readmitted to the hospitals due to the repeated occurrence of adverse drug reactions. There were complaints related to gastritis and musculo-skeletal pain like joint pains, myalgia and arthralgia, which were identified as the most commonly occurring adverse drug reactions from second-line

anti-tuberculosis drugs. Sometimes when the reactions are severe, caregivers discontinued the drugs.

"…when I discontinued cycloserine, the joint pains disappeared… [P-3M]".

During the incidences of adverse drug reactions, caregivers found at the treatment follow up centres contacted physicians at the hospitals. As such, caregivers of the treatment follow up centres managed the adverse drug reactions according to the advice they got from physicians at the hospitals. A physician mentioned that some of the adverse drug reactions like the hypokalemic tetani which are common among patients on injectables are killers. Moreover, such adverse drug reactions were reported to be difficult to detect clinically as they do not show apparent clinical signs and symptoms until they are at the advanced stage. The next excerpt illustrates this:

"…detection of electrolyte disturbance needs advanced laboratory with functional electrolyte test which we do not usually have…'"[P-5M]."

Caregivers also mentioned that except those physicians who were well experienced on the clinical management of MDR-TB and on the clinical management of drug related adverse drug reactions, others usually do not even suspect the physiological derangements that result among the patients taking second-line drugs

"…she was 21 and they told me that she was seizing with hypokalemic tetani and she went to a private clinic and they told her that she had hypertension and put her on nefidipine…, I said no!…it cannot be hypertension. When I measured her blood pressure it was normal but when her electrolyte was tested, she had severe hypokalemia with clinical hypokalemic-tetani and also hypomagnesemia, [P-5M]".

4.3.5.9. Caregivers' experience on patient management under daily observed treatment support

Some of the participants mentioned that patients were given treatment under daily observation by the health caregivers.

"…I can speak with full confidence on that... I do not have any hesitation on the daily observed treatment, we have close communication with patients at treatment follow up centres…they all have our contact address and if they encounter any problems like missing a daily drug dose, they phone us directly at treatment initiating centres… [P-5M]".

Another participant reaffirmed the same situation on the availability of reliable daily observed treatment support for the patients with MDR-TB after patients were linked to treatment follow up centres.

"…we are sure of their continuing treatment under daily observed treatment because we have telephonic contact with health caregivers working there and we discuss matters on the condition of patients. Secondly, we contact caregivers at MDR-TB catchment area meetings, where we get reports on the treatment status of each patient…, the other evidence is that our patients continue to show improvement and their lab follow ups show improvement. We also visit treatment follow up centres during the monthly MDR-TB clinical mentorships sessions… [P-6M]".

On the other hand, participants reported inconsistencies in the quality of the implementation of patient treatment under the standard daily observation, especially after patients were linked to the treatment follow up centres. This was captured in an excerpt taken form a caregiver practising at the hospital.

"…there were areas on the strengths and gaps...in some places, caregivers were concerned and they gave the daily observed treatment …but there were some places

where the caregivers filled out the register before providing the daily observed treatment … a one-week course of drugs was given to the patients' home…[P-7M]".

In the case of patients living far from treatment follow up centres, participants, who were caregivers, reported that they used MDR-TB treatment supporters from family members who signed and took a one-week drug-dose and supervised patient's taking the drugs on a daily basis at home. Some participants mentioned that if one is well-educated and made committed at the start of the treatment, the patients with MDR-TB did not opt to discontinue treatment even during events of drug side effects and other challenges. Based on these points of argument, these participants expressed their belief in the need to decentralize the daily observed treatment support to be supervised by community health workers or by family members of the MDR-TB patients. Use of family level treatment supporters were reported to be the better option especially when the patient with MDR-TB live far away from the community level treatment follow up centres.

"…when patients live far it is a serious condition…it is difficult for them to attend the daily observed treatment given at the treatment follow up centres …some patients live 8 kilometres or more away from the follow up centres and that is the main challenge we have' …[P-1M]".

However, given the fact that a huge number of tablets of each of the second-line drugs were taken by an MDR-TB patient per day, no convincing practice was mentioned by participants on the quality in which the second-line drugs that were handed over to the patients' homes were handled. Moreover, for the majority of the patients with MDR-TB who live far from treatment follow up centres, there was no reliable supportive system to ensure the quality of the daily observed treatment support given at the patients' home areas.

Furtheremore, participants mentioned that for patients coming from remote rural areas, it is difficult for them to attend the daily treatment especially when injections are taken

daily. It was reported that health extension workers who are living and working at community level were not supporting MDR-TB patients with the daily observed treatment support. The next excerpt clarifies this:

"…in our 'kebele', health extension workers are not providing daily observed treatment support and even for the susceptible TB… [P-2F]"

Thus, it was mentioned that some patients with MDR-TB were forced to rent houses in the towns of the treatment follow up centres in order to be close to the MDR-TB treatment follow up centres. Yet, participants mentioned that there was no patient support scheme by the programme of MDR-TB whereby patients from remote areas were supported with the cost of accommodation at MDR-TB treatment follow up centres.

4.3.5.10. Caregivers' experience on status of follow up laboratory services for routine patient monitoring

Participants mentioned that baseline laboratory investigations were done for all patients initiated on second-line drugs. Monthly sputum smear microscopy and culture were mentioned as the main laboratory based monitoring parameters for patients on treatment. It was mentioned that patients are also eligible for other follow up laboratory investigations like complete blood count, organ function tests and electrolyte tests. Some participants felt that the current functionality status of facility laboratory and the sample transport system are encouraging. Yet, many participants at the two study sites mentioned that there are persisting gaps in the laboratory service needed for the follow up of patients with MDR-TB.

At the level of the referral regional laboratory, there is a problem in transporting sputum samples from hospitals to regional labs where monthly culture follow ups are done for patients on treatment. Reasons mentioned were that the national postal system that was introduced for sample transport was not fully functional. Therefore, the turnaround time for the result of the sputum culture from regional labs to the hospitals was reported to be very long. Participants, who are caregivers, pointed out that the delay with culture results hampers timely clinical decision making by caregivers and contributes to the incidences of loss of life.

At the hospitals level, the shortage of laboratory reagents and failure of laboratory machines were reported as the main factor limiting patients' access to the standard laboratory follow up services. Repeated failure of electrolyte machines and the lack of local capacities to maintain them promptly, were mentioned as examples for the causes of the problems in laboratory services. Moreover, lab tests on hormonal assay like the thyroid function test, are totally unavailable.

"…due to lack of reliable follow up laboratory services for prompt diagnosis and treatment of treatment related adverse effects, there were problems like the incidence of a sudden death of patients, and thus both as an individual and as a physician treating the patients, I am feeling the pain…[P-7M]".

The other factor mentioned regarding laboratory related problems was the lack of cooperative team work between the caregivers and the hospital laboratory personnel. Participants noted that as not enough attention was given to the programme of MDR-TB by the hospital management, there was no cooperation from the hospital laboratory personnel in collecting and processing samples of the patients with MDR-TB.

"…they rejected the lab requests we made and did not process them,…unless they were paid for that, they are not cooperative…[P-5M]".

Similarly the other participant mentioned this:

"…they did not collect, label and pack samples properly …so the samples got lost while on transit …[P-2F]".

Moreover, caregivers for MDR-TB perceived the shortage of laboratory human power at hospitals as another problem. As it happened, available laboratory personnel were occupied with providing routine services for the general hospital polyclinic attendants. Thus, it was reported that the hospital laboratory services which was originally established for providing services for the general hospital polyclinic could not adequately provide the routine laboratory services needed for the patients with MDR-TB. Therefore, participants who were caregivers recommended for the need to establish a laboratory unit which is dedicated to the MDR-TB treatment centres of the hospitals.

4.3.5.11. Caregivers' experience on the social and economic challenges posed by MDR-TB on patients with the disease

4.3.5.11.1. The social impact of MDR-TB on the patients with the disease

Participants at the interviews mentioned that a substantial number of patients treated for MDR-TB were those living in desperate economic and social conditions. The participants reported that there was a stigma attached to them and there was discrimination against patients with MDR-TB. The stigma is not only against the patients with MDR-TB but it is also against the caregivers for MDR-TB. There is huge fear both by the community and particularly by the health care givers regarding the MDR-TB disease.

"…MDR-TB is seen as something strange and is seen as a disease not found in other places on earth,… both caregivers working there and the MDR-TB patients are perceived as strange persons,…MDR-TB caregivers themselves are stigmatized by co-workers in the same way as the MDR-TB patients are.…"[P-7M].

Thus, participants recommended that the health system should consider MDR-TB and integrate its services into the care and services given on chronic diseases like diabetes.

Patients with MDR-TB, as noted, were also stigmatized by the community. When patients with MDR-TB are known to the community, they are discriminated against and are systematically separated from routine social life and from work.

4.3.5.11.2. The economic impact of MDR-TB on the patients with the disease

There were patients who lost their lives to the combined problems of MDR-TB, lack of adequate food, finance and social support. There were patients living alone and had no one to take care of them and help them especially with food. Some participants mentioned that there were very poor patients whose treatment for susceptible tuberculosis failed and were put on second-line anti-tuberculosis drugs. Still, such patients took second-line drugs in very poor living conditions and caregivers felt that response to treatment by such patients was not encouraging.

"… he is 46 and he failed to gain weight,…he also had his own social problems with food and finance and in all aspects,….he had a daughter who had been taking care of him but she died last September, now he is readmitted to the hospital…his kidney is failed and moreover he has hypokalemia,…[P-1M]."

Participants also reported that poverty challenges patients' ability to adhere to the treatment given for MDR-TB. For example, during the outpatient phase of the treatment, patients were expected to attend the daily injection and daily observed treatment at the treatment follow up centres or health centres. For most patients who were coming from remote rural areas, treatment follow up centres were described to be very far from patients' living homes. Such patients had to pay for house rent at the home town of the treatment follow up centre. As there was no accommodation allowance for patients linked to the treatment follow up centres, the condition was reported as an additional challenge for the poor patient with MDR-TB.

4.4. Results for the mixed methods objectives component

4.4.1. How the interviews with patients with MDR-TB help to explain quantitative results.

4.4.1.1. The socio-economic impact of becoming a patient with MDR-TB

The quantitative component of the study revealed that 128 (94%) of the patients were in the productive age group (age group of 15-64 years). Yet, the majority 70 (53%) of the patients with MDR-TB were self-employed mainly in the informal sector, and a considerable number 46 (35%) were not employed. The 70 (53%) of patients who were employed, were either self-employed or employed in the informal sector.

The interviews with patients revealed that self-employment was employment in the daily labour workforce whereby daily wages were paid. Participants reported that physical strength is needed to be employed in the daily labour workforce. As such, the participants highlighted that patients with MDR-TB were often unwell because of the disease and thus could not continue to work or perform their daily functions in their daily labour work as expected. Thus, patients encountered financial problems and the associated problems when they lost jobs as a result of the disease. On the other hand, participants mentioned that the social support offered to patients with MDR-TB by the MDR-TB programme in the form of nutrition and financial support was inadequate. Hence, the results of the qualitative component of this study clearly indicated that the majority of patients with MDR-TB were living in poverty. The next excerpt clarifies this:

"…yes before, I used to cater for myself by running here and there. But after I was diseased there was a problem, people had a negative attitude towards me and also I did not have the strength to work as I used to …I had to accept the food that I was given from here. I could not do or say anything but accept it. What could I do after all?…it was the same thing for the whole month!... no it was not enough…some patients may get support from parents or relatives, but for others the food we are given by the hospital cannot be enough for one month…[P-2M].

4.4.1.2. Treatment outcomes of patients with MDR-TB

The results of the quantitative component revealed that from the total of 110 patients for whom treatment outcomes were assigned, 76 (69%) of the patients had successfully completed the treatment given for MDR-TB. However, 30 (27%) of the patients enrolled to treatment died from the disease by month 24. Thus, death was found to be the second higher treatment outcome among patients with MDR-TB enrolled to treatment at the two study sites.

The qualitative in-depth interviews conducted with patients with MDR-TB, clarified the dynamics in the process of MDR-TB treatment that were associated with patients' deaths. Participants attributed the deaths to the seriousness of the MDR-TB disease itself and the difficulty of adhering to its treatment. Participants mentioned that some patients with MDR-TB are repeatedly admitted to the hospitals due to drug related adverse events and other complications. Some of the patients who encountered treatment related complications and were readmitted to hospitals, were died of the disease. An excerpt taken from a patient on treatment who survived severe adverse drug-reactions from the second-line drugs, clarified how the patient lost many of his fellow patient cohorts due to the disease:

"…thanks to God that now I am attending to the treatment alive,…when I came the first time, I was very weak,…the doctor advised me to take the drugs and then my condition improved and I got up from the bed,… from patients who were admitted with me to this hospital for treatment, …out of five of us who were admitted at the same time to this hospital, only two of us were discharged alive and three patients died from the disease before they were discharged. Also, there were many patients who were died but for me, may my God be blessed that now I am attending the treatment and I am alive,…[P-4M]".

The above excerpt states an eye witness account and the lived experiences of the patients that the disease, MDR-TB, is perceived as a deadly disease.

4.4.1.3. MDR-TB infection control

The quantitative component of the study revealed that 105 (77%) of patients with MDR-TB were linked to the community level MDR-TB treatment and follow up services. On the other hand, an analysis of the community level MDR-TB infection control practices of the caregivers revealed that for all patients linked to the community level MDR-TB treatment, there were no housing arrangements made before the patients were linked to the community. This meant that caregivers at the treatment follow up centres did not visit patients' homes to inspect patients' living quarters and educate the family members on the dangers of MDR-TB transmission to household contacts. The caregivers did not implement the community level MDR-TB infection prevention and control practices that were strictly recommended by the national guideline for community level MDR-TB treatment and patient care (Federal Ministry of Health/FMOH/ 2014:150-51). For example, for 64 (47%) of the patients with MDR-TB who were on treatment, MDR-TB infection control services were not given through contact tracing. Thus, 8 (6%) of the total of the 136 patients included in this study were those diagnosed from the household contacts of the index patients with MDR-TB.

The qualitative interviews with patients revealed that patients did not have insight about the risk of MDR-TB infection and its transmission to their close contacts and household members. The reason mentioned was the absence of adequate education on the danger of MDR-TB transmission from patients to their household and close contacts. The excerpt taken from a patient on treatment elucidated this:

"…I caught the disease while I was taking care of my husband. I had never had TB before... he was my husband…while I was taking care of him, I did not know about the disease because both of us did not have this disease before. They put him on the six-month treatment and at that stage, they did not tell us about any precautions, and no advice was given for him also. When he started the treatment, I did not think that the disease transmits and in fact he is my husband and I could not abandon him because he was sick and I could not go away. If we were told that it transmits, I would have taken care and he also would have taken care of me…[P-6F]".

The above excerpt makes it clear that patients with MDR-TB and their families were not given the information they needed on MDR-TB.

Moreover, the patients with MDR-TB who participated in the study reported that the education given to the general public on MDR-TB was inadequate. A participant noted that patients had the interest to teach the public about MDR-TB and the challenges associated with taking the treatment given for it. An excerpt taken from a patient participant illustrates this.

"…having passed through many challenges, about this disease let alone my family but the whole society if there is someone who takes the message from me I am very interested to teach others and to share the experience I passed through so far… So if the public learns and knows the problem, the public will not be hurt by the disease [P-5F].

The quantitative result identified the risk of MDR-TB transmission to the community due to the unregulated practice of patient transportation from hospitals to the community and back to the hospitals for the scheduled monthly follow up services. During the initial patient linkage to the community, only 97/105 (71%) of the patients were transported from treatment initiating centres (hospitals) to treatment follow up centres using hospital ambulances. The rest of the patients with MDR-TB were left to use public transport starting from the inception of their treatment.

A more elaborative understanding on patient transport was obtained from the results of the qualitative component of the study on the practice of patient transport. Participants (caregivers) reported that patient transport using the hospital ambulance was provided only during the initial patient linkage to community level MDR-TB treatment and follow up centres. After the first patient linkage to the community, patients use the conventional public transport services for the whole duration of the two years' treatment period for whatever movements they make to seek care for MDR-TB. These movements included attendances to the programmatically scheduled monthly clinical follow ups at the hospitals and the daily movements that patients make

between their areas of residence to the treatment follow up centres for collecting daily drug doses. The excerpt below, taken from a physician who was caring for patients with MDR-TB, clarified the risk of MDR-TB infection to the community as a result of unregulated patient movement during the course of their treatment:

"…When they go from here to the treatment follow up centres, we cannot say hundred percent. There are patients transported by ambulance for the first time. But as there are not adequate numbers of ambulances, they go by public transport. We advise them on what we can advise them and what they should do. But the ambulance is not available most of the time…[P-5M]".

Thus, the study revealed that the inadvertent patients' movement to take their daily treatment and to attend to their monthly clinical follow up services at the hospitals is a potential risk in transmitting MDR-TB to the general public. Even though they could not easily avoid the risk of the disease transmission to the community, patients with MDR-TB well understood the danger of the disease to the public.

"…the disease is not something that is seen as an ordinary disease even for myself I usually get stressed with the disease when I approach others. In fact, I should take care of others, I get stressed about how difficult it is to take the drugs. The drugs are very hard, I for example, usually feel pain when I take the drugs… as an Ethiopian citizen I caution that this disease is not easy a disease to deal with. It is good that the government treats patients in one dedicated centre and persons go back to the community after completing their treatment, otherwise we may infect others … [P-9M]."

4.4.2. How the interviews with caregivers help to explain quantitative results

4.4.2.1. Management of MDR-TB and HIV/AIDS co-infected patients

The result of the quantitative component revealed that 34 (26%) of the patients with MDR-TB were co-infected with HIV/AIDS. Yet, the quantitative result could not identify how patients with MDR-TB those co-infected with HIV were managed for both diseases. However, the qualitative component revealed the dynamics of the management of patients co-infected with both MDR-TB and HIV/AIDS.

Caregivers for MDR-TB mentioned that there is a higher level of MDR-TB and HIV co-infection among patients treated for MDR-TB. However, the services for both MDR-TB and HIV/AIDS were not available in one centre. Caregivers at the MDR-TB centre did not have the training to prescribe anti-retroviral drugs for patients co-infected with HIV/AIDS. Moreover, the MDR-TB centres did not have the supplies of the anti-retroviral drugs.

Caregivers attribute the higher level of death observed among MDR-TB and HIV co-infected patients, included in this study, to the absence of an optimum continuum of care and follow up services that patients affected by both MDR-TB and HIV/AIDS needed. A physician, who was treating MDR-TB and HIV/AIDS co-infected patients, desperately narrated the incident of a sudden death that occurred to an MDR-TB and HIV/AIDS co-infected patient in the 17th month of his treatment for MDR-TB.

"…the patient was on anti-retroviral therapy for seven years and then he caught MDR-TB and was on treatment for MDR-TB for 17 months. The patient focused on the new problem of MDR-TB and the challenges associated with taking both second-line and anti-retroviral drugs. In such scenarios, the patient's anti-retroviral clinic did not provide the routine laboratory evaluation that the patient needed to make sure of the continued success of the anti-retroviral therapy in suppressing the patients' viral load. While hopefully completing his MDR-TB treatment, one day the patient suddenly fell in the road and comatosed. Then the patient was taken to the hospital where the MDR-TB treatment was initiated. The patient was evaluated at the MDR-TB treatment centre

and it was discovered that his T-lymphocyte cell bearing (CD4) count was only 40 cells per cubic millilitre which indicated failure of the patient's anti-retroviral treatment and that may have been the possible cause of the patient's death,…the anti-retroviral therapy failure was not diagnosed until the patient was found fallen down on the road,….[P-5M].

As the patients who were MDR-TB and co-infected could not get optimum follow ups and care for the HIV disease from the MDR-TB centre, patients were obliged to visit another facility and another caregiver to get care and treatment for the problem of HIV/AIDS. An excerpt taken from a caregiver also illustrates the grievances that patients encounter due to the absence of integrated care for MDR-TB and HIV/AIDS in one centre.

"…for the HIV problem, patients' main follow up centre is the anti-retroviral therapy clinic. When there are problems, we refer patients to the caregivers for HIV/AIDS,… [P-8M]".

4.4.2.2. Management of adverse drug reactions from second-line anti-tuberculosis drugs

The quantitative component of this study revealed that, adverse drug reactions from second-line drugs, among patients included in this study, were common. It was shown that all of the 91 (100%) patients with MDR-TB for whom data on adverse drug reactions were available, experienced at least one episode of adverse drug reaction in the course of their treatment for MDR-TB. moreover, from the total of the 91 patients, 31 (34%) of them experienced five or more episodes of adverse drug reactions from second line drugs.

An analysis of the patients' access to routine laboratory follow up services showed only 15% of the patients enrolled to treatment had access to the standard follow up laboratory services recommended by the World Health Organization and that adopted by the Programmatic Management of MDR-TB in Ethiopia. Thus, the majority of the

patients on treatment were not getting the programmatically recommended routine laboratory follow up services.

The qualitative component of the study, through the interviews with caregivers, clarified the dynamics around patients' access to the standard laboratory follow up services recommended for patients with MDR-TB while on treatment. The status of patients' access to the basic diagnostic and follow up laboratory services was elaborated in the actual context of the study sites. It was revealed that the hospital MDR-TB treatment units lacked laboratory units dedicated for patients treated for MDR-TB. The hospital MDR-TB treatment units shared the hospital general laboratory facilities which were originally established for providing services for the general hospital polyclinic; which could not adequately provide the routine laboratory services needed for patients with MDRTB. It was clarified that absence of dedicated, comprehensive and consistently functional laboratory challenged the process of clinical decision making in many ways. The caregivers mentioned that the majority of the patients with MDR-TB develop adverse drug reactions in the course of their treatment for the disease. It was made clear that some of the adverse drug reactions were easily diagnosed using clinical signs and treated accordingly. Yet, for some of the adverse drug reactions, the diagnosis needs routine laboratory follow up tests.

As such, caregivers mentioned that some of the adverse drug reactions which are difficult to diagnose clinically usually go unnoticed and lead to severe complications which can be fatal. At the rural treatment follow up centres, adverse drug reactions from second-line drugs were not diagnosed early or they were usually misdiagnosed and mistreated. As a result, patients with MDR-TB usually encounter clinical complications from adverse drug reactions and are readmitted to the hospitals for treatment. The next excerpt was on a patient's story narrated by the physician caring for her in which absence of advanced lab tests challenge early diagnosis and prompt management of adverse drug reactions from second-line drugs.

"…The practical challenges are, firstly for the drug side effects, the chance to clinically detect them is very difficult. Many of them are known through advanced laboratory diagnosis like for example, the electrolyte analysis and it is a very big killer problem.

You may not detect it symptomatically, I mean until it is in the advanced stage. These things, especially at treatment follow up centres are challenging. They cannot be detected without laboratory tests. I can mention one patient as an example. She developed hypocalcemia and what she did was, as she has money, she went to a private clinic. When she got there, they told her that it is hypertension and they gave her anti-hypertensive drugs. She was seizing, the problem was hypocalcemic tetani. But, they made her start on nefidipine. She is 21 years old. At that time, I called a catchment area meeting. Then when we were talking, they told me that the patient was diagnosed with hypertension and she is admitted. I told them this could not be hypertension and I asked them to bring the patient to me on the next day and I told them that I would admit her and follow her up. Then, she was admitted. When we followed up, her blood pressure was normal. Meanwhile, had developed hypocalemic tetani. When we measured it, it was severe hypocalcemia with hypokalemia and hypomagnesemia. The symptomatic identification of these side effects is challenging, it is very difficult to detect them. Even at our hospital electrolyte test is not done…especially these days nothing is done at our laboratory. At one time there was reagent shortage. The other time, laboratory technicians were not cooperative. We took the sample and they told us that the sample had expired. But most of the time they say the machine is not functional. Most of the time it is reagent and the machine, that created very huge problem,… …[P-6M]".

The quantitative component revealed that all the 91 patients with MDR-TB for whom data were available on adverse drug reactions from second-line drugs experienced at least one episode of adverse drug reactions. On the other hand the qualitative inquiry through interviews with caregivers revealed that the ancillary drugs used to treat adverse drug-reactions from second-line anti-tuberculosis drugs were not consistently available through the national programme of MDR-TB. Instead, the hospital MDR-TB centre uses the routine hospital pharmacy stores to get ancillary drugs for patients with MDR-TB who need treatment for adverse drug reactions. The next excerpt clarifies how caregivers use different mechanisms to get ancillary drugs for patients:

"…the problem of ancillary drugs, what we do at our hospital is that we discuss the problem with the main hospital pharmacy, we as caregivers do this as the programme is our responsibility and as it this is our own issue,… we reached an agreement and we take drugs from them and give the drugs to the patients…patients get drugs for free,…[P-5M"].

4.4.2.3. Patients' attendance to the daily Directly Observed treatment schedule

The quantitative component of this study revealed that, from the total number of patients with MDR-TB included in this study, data on the patient's attendance at daily observed treatment were available for 93 (68%) of the patients on treatment. The assessment of patients' level of attendance at daily Directly Observed treatment revealed that there was evidence of strict daily observed treatment attendance by 53 (57%) of the patients. For this group of patients, there was no evidence of missed daily drug doses.

The interviews with caregivers revealed that efforts were made to make sure that patients take their daily treatment under observation. Such efforts were made both for patients treated at the hospitals and those linked to the community level MDR-TB treatment and follow up centres. For patients linked back to the community after treatment initiation at hospitals, patients were given contact addresses of the caregivers found at the hospitals (the treatment initiating centres). Patients were told to contact their hospital level caregivers if they encounter any problem at the treatment follow up centres. This was described by an excerpt taken from a physician treating patients with MDR-TB:

"…As a practicing physician I can speak with full confidence on that…once we send patients from here to the community, we have communication with caregivers at the treatment follow up centres and we confirm if the patients have reached them… In addition, all patients have my cell phone. They personally phone me. If the caregiver is absent, the patient himself calls me. Patients themselves phone me even before caregivers at the treatment follow up centres call me and they tell me if they missed the drug dose of the day…. not only this, when we call for the catchment area meeting,

we get the full report of patients treated at follow up centres. If there is something beyond their capacity, if adherence problem is encountered, we agreed that if a patient misses a one-day drug dose, we have to know on the second day. If they encounter any problem, they will tell us…, maybe that is the main reason for the low rate of lost to follow ups in our case…[P-5M]".

Yet, there were patients who did not strictly adhere to the scheduled daily treatment under the direct observation of a treatment supporter. For the 28 (30%) of the patients, adherence or attendance to the daily observed treatment was poor and there was evidence of missed daily drug doses. For some 12 (13%), patients adherence or attendance to the daily observed treatment was irregular or erratic.

The quantitative result also revealed that 53% of the patients were self-employed in the informal sector mainly in the daily labour work space while 35% of the patients were not employed at all.

The qualitative part of the study has clarified the dynamics at play around the patient's attendance to the scheduled daily treatment under direct observation by a treatment supporter. The qualitative result revealed that, patients with MDR-TB face social and financial hardships due to the inadequate income they get. Most patients could not strictly adhere to the conventional daily labour work as a result of losing their physical strength to the disease, MDR-TB. On the other hand, the service on patients' treatment under the daily direct observation was not formally decentralized beyond the treatment follow up centres. The reason for that, as was mentioned by caregivers, was that there is lack of involvement by the community health extension workers in the provision of daily treatment support for patients with MDR-TB those linked to the community. A nurse caregiver for MDR-TB mentioned the lack of involvement of the health extension works in MDR-TB treatment support as follows:

"… the community health extension workers providing the daily observed treatment support for patients with MDR-TB, No! There is no such practice in our situation, I do not know what happens at other places,…[P-1M]".

As clarified in the above, a combination of socio-economic problem and absence of strictly patient centred daily observed treatment support challenges patients' coping ability to the standardised schedule of treatment under daily observation.

4.4.2.4. Community level MDR-TB infection control

From the quantitative data, it was found that for all patients linked to community level MDR-TB treatment support (n=105), no housing arrangement was prepared before the patient was linked to the community. For these patients, no household level MDR-TB infection control arrangements were made. It was also found that from the total of 136 patients with MDR-TB included in this study, 8 (6%) patients with MDR-TB were diagnosed from household contacts of the index patients with MDR-TB

The result of the interviews with caregivers for MDR-TB supported the quantitative result on community level MDR-TB infection control. Caregivers found at the treatment follow up centres were not visiting patients' homes to make arrangements for MDR-TB infection prevention at the patient's household level. As such, families of the patients with MDR-TB and the surrounding community were not getting information and insight about the disease.

The qualitative interviews with patients revealed that patients who contracted MDR-TB from household members did not have insight about the risk of MDR-TB infection and its transmission to their close contacts and household members. The reason mentioned was the absence of adequate education on the danger of MDR-TB transmission from patients to their household and close contacts. The excerpt taken from a patient on treatment elucidated this:

"…I caught the disease while I was taking care of my husband. I had never had TB before... he was my husband…while I was taking care of him, I did not know about the disease because both of us did not have this disease before. They put him on the sixmonth treatment and at that stage, they did not tell us about any precautions, and no advice was given for him also. When he started the treatment, I did not think that

the disease transmits and in fact he is my husband and I could not abandon him because he was sick and I could not go away. If we were told that it transmits, I would have taken care and he also would have taken care of me⋯[P-6F]" .

Moreover, some of the patient participants of the interviews mentioned that the wider community lacked adequate insight about MDR-TB. Thus, patient participants reported that because the people around them do not have information about MDR-TB, the responsibility of caring for others rests on the patient.

"…I refrain from mixing with people… they say 'he refrains from us because he might be losing hope ...'… the community knows nothing about the disease….it is very important that the public is taught on this problem…[P-4M]".

It was also reported that the effort of patients to care for others in order to prevent the transmission of the disease MDR-TB fades with time. This might be due to the absence of ongoing efforts to encourage and support patients and their families on the continued need for the prevention of MDR-TB infection.

"… in our family we use masks for one or two months and then we may stop using the masks and start living without the mask…[P-9M]".

As a way out for preventing the risk of MDR-TB infection to the larger community, some of the participants of the interviews recommended the need to treat patients with MDR-TB in a dedicated centre where patients can complete the entire treatment given for MDR-TB before going back to the community. Caregivers mentioned multiple problems hindering the smooth implementation of community level treatment of MDR-TB. The factors mentioned were the absence of strong monitoring by the respective health management, inadequate commitment by caregivers at the treatment follow up centres and inadequate logistic arrangement, like motor bics, to visit every patient's home. These problems were perceived to contribute to the transmission of MDR-TB among

household contacts. A nurse providing clinical care for patients at a hospital mentioned the problem as follows:

"…By the way, tuberculosis, as it is well known, is a disease of the poor. I mean, I think you understand me, there are many issues like well-ventilated living rooms, there are many, many factors, there are gaps in quickly picking up and diagnosing those with a two weeks cough; I mean we see it in general. Additionally, we see that from the side of TB patients, after you have diagnosed them, there is problem with providing daily observed treatment services,…[P-3M]".

4.5. Summary

This chapter has presented the results of the quantitative, qualitative and that of the mixed methods objectives. The next chapter, chapter 5, presents the steps used for the development of the model for enhancing the treatment of patients with MDR-TB in Ethiopia. Moreover, chapter 5 presents the application of the various components of the model for enhancing the management of patients with MDR-TB.

Chapter 5: Model development

5.1. Introduction

The previous chapter presents the result of the study. This chapter is on the development of a model for enhancing the management of patients with MDR-TB. The conceptual model is developed using the results of the study, expert opinions, the researcher's clinical experience and the extant literature.

5.2. The key concepts of a model

5.2.1. Definition of a model

A model is a symbolic representation of concepts or variables and the interrelationships among them (Jaccard & Jacoby 2010:28-9). A model is a conceptual basis for how a programme is supposed to work. It can be presented as a figure or as a text. It serves to objectify and present key aspects of a programme, including the functions of those aspects (Modest & Tamayose 2004: 85-6).

5.2.2. Elements of a model.

Based on the literature review, models are made up of variables, constructs and theory. A theory is an interrelated set of constructs that specify the relationship among variables. Theories help to explain or predict phenomena that occur in the real world (Creswell 2009:51-2). Constructs are higher order concepts that are constructed from concepts. Constructs enable us to have an understanding of the real world. Constructs encompass a universe of possibilities. Yet, constructs often lack clarity. Thus, constructs need to be expressed in a way that is clear and precise so that it can be shared (Jaccard & Jacoby 2010:12-13).

When a construct is assigned a specific property and can be measured it is called a variable. Variables are characteristics of individuals or organizations that can be measured or observed (Fertman & Allensworth 2010:59-60). Variables are important because entities in the real world differ depending on differences in the variables that describe them (Jaccard et al 2010:13). The value of each of these variables affects the systems' functional state. If any of the variables changes in some way, it affects

the entire function of the system (Reid, Compton, Grossman and Fanjiang 2005:37-38).

In a healthcare system, a model helps to guide addressing a specific health problem or health events (Fertman et al 2010:433). A model of healthcare defines the way health services are delivered. In other words, through the application of a set of service principles; a healthcare model outlines the best practice for the delivery of care for the patient (Government of Western Australians 2006:4).

5.2.3. General approach to model building

In the Western countries, systematic analyses of the quality and cost effectiveness of healthcare have been done for decades. Use of the condensed information from such analyses has helped in the development of guidelines and practice standards. Use of these guidelines and best practice information by healthcare practitioners has enabled them to improve the quality and cost-effectiveness of the care they give to their patients. The Joanna Briggs Institute (JBI) model of evidence-informed healthcare is the best example of the identification, appraisal, syntheses and use of the best available research evidence to inform and improve health services. As a form of decision making, the process of evidence-informed practice involves evidence generation, evidence synthesis, evidence transfer and the utilization of the evidence in routine clinical care (Pearson, Field & Jordan 2007:6). As such, the basic steps for the development and application of a model for healthcare include understanding the policy context, understanding the current state of practice (evidence) and translating evidence into best practice using the model of care. Models of care can be developed for diseases, conditions or population groups that deliver services that meet both community health needs and nationally set health outcomes.

5.2.4. Evidence generation

The first step in model development is often the generation of ideas about the explanatory constructs and the relationships among them regarding the phenomena that one tries to explain. Then ideas generated are subjected to more careful analytic scrutiny to elaborate on more promising ideas that are pursued further (Jaccard & Jacoby 2010:39-40). As such, healthcare evidence generation is the first step in the

process of evidence-informed practice. This is because it is difficult to have evidence-informed practice without evidence. Evidence is the basis for belief. Evidence is the substantiation or confirmation that is needed in order for us to believe that something is true. Regarding healthcare, evidence can be generated about different segments of a healthcare. These include the feasibility, appropriateness, meaningfulness and effectiveness of the evidence.

5.2.5. Evidence synthesis

Evidence synthesis is the second step in model development. It concerns the analysis of research evidence and opinions on specific topics of interest. In other words, evidence synthesis involves the pooling of research findings. The pooled research findings help to effectively determine the interventions, activities or phenomena that the evidence supports. There are certain core elements in the process of evidence synthesis. The development of a theoretical understanding of the nature of the reality together with the role of evidence in healthcare forms an important element of evidence synthesis. Moreover, operationalization of the evidence synthesis and the systematic review of the relevant literature on a particular condition form other crucial elements of evidence synthesis. Evidence synthesis entails the integration of results that are obtained through various methods. A pluralistic approach to evidence synthesis involves the analysis and use of evidence generated via both quantitative and qualitative inquiry (Pearson, Field & Jordan 2007:21-2). Moreover, data interpretation needs to reflect both statistical significance and its importance to stakeholders. Thus, the summary of the information will help to present a balanced report that addresses the value of the phenomena to the different stakeholders (Harris 2010:133). Quantitative result may be synthesized using statistical analysis. It measures the effect of the predicator variable on the dependent variable. Qualitative results are synthesized to create the summary of the meanings of the phenomenon under study. In the development of the model for enhancing the care of patients with MDR-TB, the various segments of the research results were combined logically and reasonably. Study results that reflect relationship among phenomena are put in category so as to reach a coherent whole that can inform practice. Evidence synthesis facilitates decision making in healthcare.

5.2.6. Transfer of evidence or knowledge

This is the third step in model development. This component of model building is concerned with the act of transferring knowledge to individual health professionals, health facilities and the healthcare system. This is done through publications, electronic media and other decision support systems. Knowledge transfer is more than the dissemination of information. It needs careful identification of strategies that identify the target audience such as clinicians, managers and policy makers and consumers and the design, packaging and transfer of information that is comprehensive and useable in decision making. Effective knowledge transfer entails an understandable and audience appropriate message that is conveyed through organizational systems in a cost effective way.

In the development of the model for enhancing the programmatic management of patients with MDR-TB, the target audiences in the programmatic management of MDR-TB were identified. These include all level clinicians providing care for patients with MDR-TB, programme managers at hospitals and the general health care management within the regional health bureau and policy makers. For these actors, the model developed represents the evidence or knowledge transfer component. The model has educational and information delivery role for programme managers and caregivers in the programme. As such, transfer of evidence to those who are in a position to implement the knowledge in practice is central to the evidence-informed process. Moreover, the result of this study will be disseminated to individual health professionals globally by means of journals and other electronic media.

5.2.7. Evidence utilization

This is the fourth step in model development. Evidence utilization is the implementation, in practice, of the evidence or knowledge possessed by healthcare professionals. In the context of the current study area, the gaps in the implementation of the programmatic management of MDR-TB was identified by each level or component of the programme. In the model, each component was described and its application to enhancing the programmatic management of patients with MDR-TB was clarified. Such implementation of evidence in practice helps to change the routine care

practices. Through changing organizational practice, evidence utilization will ultimately impact the process of care and health outcomes. Moreover, utilization of evidence helps to base routine practice on best available evidence. It also addresses the context in which the care is given, client preferences and professional judgement of caregivers. In this view, the model developed to enhance the management of patients with MDR-TB will serve as a vehicle to drive the required change to mitigate the gaps in the management of patients with MDR-TB.

5.3. Data sources for the development of the model

Data for the development of the model for enhancing the care of patients with MDR-TB were gathered from different sources. These sources included the literature reviewed, results of the study on the treatment outcomes of patients with MDR-TB and its determinants and the researcher's own experience on the programmatic management of MDR-TB in the Ethiopian context.

5.3.1. The literature review

Development of a conceptual model depends on the powers of observation, grasping a problem of interest and knowledge of prior research results. The observations are often the results and conclusions of a research endeavour (Polit & Beck 2003: 132). As such, a critical analysis of the available literature is intrinsic to concept analysis (Yazdani & Shokooh 2018:34). The literature review is a process of presenting theoretical explanation for the variables and constructs under investigation (Sumerson 2014:45).

In this study, the literature review was used to identify theories and ideas for the research. Guided by a conceptual framework, the boundary to the scope of the literature search was set by the aims, objectives and the hypotheses of the study (Crano, Brewer & Lac 2015:5-6; Imenda 2014:186). The adopted framework of the study, the Donabedian framework, enabled the researcher to assess a range of factors associated with the treatment of patients with MDR-TB and with the quality of the care given for patients with MDR-TB (Donabedian 2005:695). The literature identified important ideas and concepts on the treatment outcomes of patients with MDR-TB and its determinants. Thus, the concepts synthesized through the literature review were

used to develop the model for enhancing the care of patients with MDR-TB and patients' satisfaction with care given for MDR-TB.

5.3.2. The research result

The result of the study has enabled the researcher to identify the clinical and programmatic system related determinants of the outcomes of patients with MDR-TB, patients' perceived quality of care and patients' satisfaction with the care they receive for MDR-TB. These factors are a potential risk for the unfavourable treatment outcomes of patients treated for MDR-TB. The research result has revealed a list of the potential risk factors for the unfavourable treatment outcomes of patients treated for MDR-TB and patients' satisfaction with the care they receive on MDR-TB. The result of the study has led to the development of insight into the clinical and non-clinical (economic, social, psychosocial) factors that determine the process and outcome of patients treated for MDR-TB. The quantitative result captured the socio-demographic and socio-economic characteristics of the study participants. The quantitative result also identified the status of the treatment outcome of patients with MDR-TB and the factors associated with the observed level of the treatment outcomes of patients treated for MDR-TB. On the other hand, the qualitative in-depth interviews with patients with MDR-TB and their caregivers, revealed factors that might determine patients' perceived quality of the care provided for MDR-TB and the satisfaction of patients with the care given for MDR-TB. The qualitative inquiry also led to an understanding of caregivers' and the patients' perceived facilitators and barriers to the management of the patients treated for MDR-TB. In summary, the results of this study contributed to the development of the conceptual model of the study.

5.3.3. The researcher's own experience

The clinical and programmatic experiences of the researcher were used in the synthesis of the evidence generated from the literature and the study results. The researcher's experience was also used during the structuring of the model developed for the management of patients with MDR-TB. Moreover, the comments obtained from the researcher's supervisor and from experts who reviewed the sections of the research result were used in the synthesis and the structuring of the model developed.

5.4. Approaches used for concept analyses for model development

The Walker and Avant (2011:58) strategy for concept identification and analyses was used to analyse and synthesise the concepts used in the development of the model for enhancing the care of patients with MDR-TB. The practice of concept analysis is an essential step to understanding logical thinking related to the terms and their meanings and their use in model development (Brush, Kirk, Gultekin & Baiardi 2016:160-1).

According to the Walker and Avant strategy, the development of a conceptual model begins with the identification of key concepts relevant to the problem of interest. It is from the key concepts that one can move to the identification of the interrelated variables or attributes of these concepts (Zeng, Sun, Gary, Li & Liu 2014:6731). Concept analyses is an analytical method used to gain an understanding of the concepts or phenomena of interest. Concepts are created by words that enable people to communicate their meanings to the world, and they provide meanings to the phenomena that are experienced directly or indirectly (Bousso, Poles & Cruz 2013:142). In this study, the main purpose of concept analyses is to develop a conceptual model for clinical decision making in the care of patients with MDR-TB in the Oromia Region of Ethiopia and the other regions of Ethiopia. The model helps to demonstrate the concepts of interest and their defining attributes.

The concepts used in the model development and their attributes were synthesised from different sources including the literature review, study results and the researcher's own experience. The literature enabled the researcher to get a thorough understanding of the problem under investigation. In the literature, factors relevant to the treatment outcomes of patients with MDR-TB, patients' perceived quality of care and patient satisfaction with care given for MDR-TB are defined explicitly. Moreover, the specific attributes of each of the major concepts are explicitly defined. From the literature, concepts most relevant to the treatment outcomes of patients with MDR-TB include the socio-demographic and socio-economic characteristics of patients with MDR-TB. Clinical conditions including adverse drug reactions from second-line drugs and co-morbid conditions with MDR-TB are concepts most cited in the literature. Likewise, concepts relevant to the patients' perceived quality of care and patients' satisfaction

with the care given for MDR-TB were patient-caregiver communication and the quality of care. Added to this, the duration of treatment, the effect of stigma and discrimination on patients with MDR-TB, status of available psychosocial and economic support, the service setups and the caring practice of caregivers were concepts relevant to patients' satisfaction with care given for MDR-TB.

The above concepts were analysed, re-structured or re-named in some instances using the framework of Walker and Avant (2011) approach for model development. The outcome of the analysis and re-structuring was a conceptual model to offer guidance for clinical practice in the programmatic management of patients with MDR-TB in the context of Ethiopia.

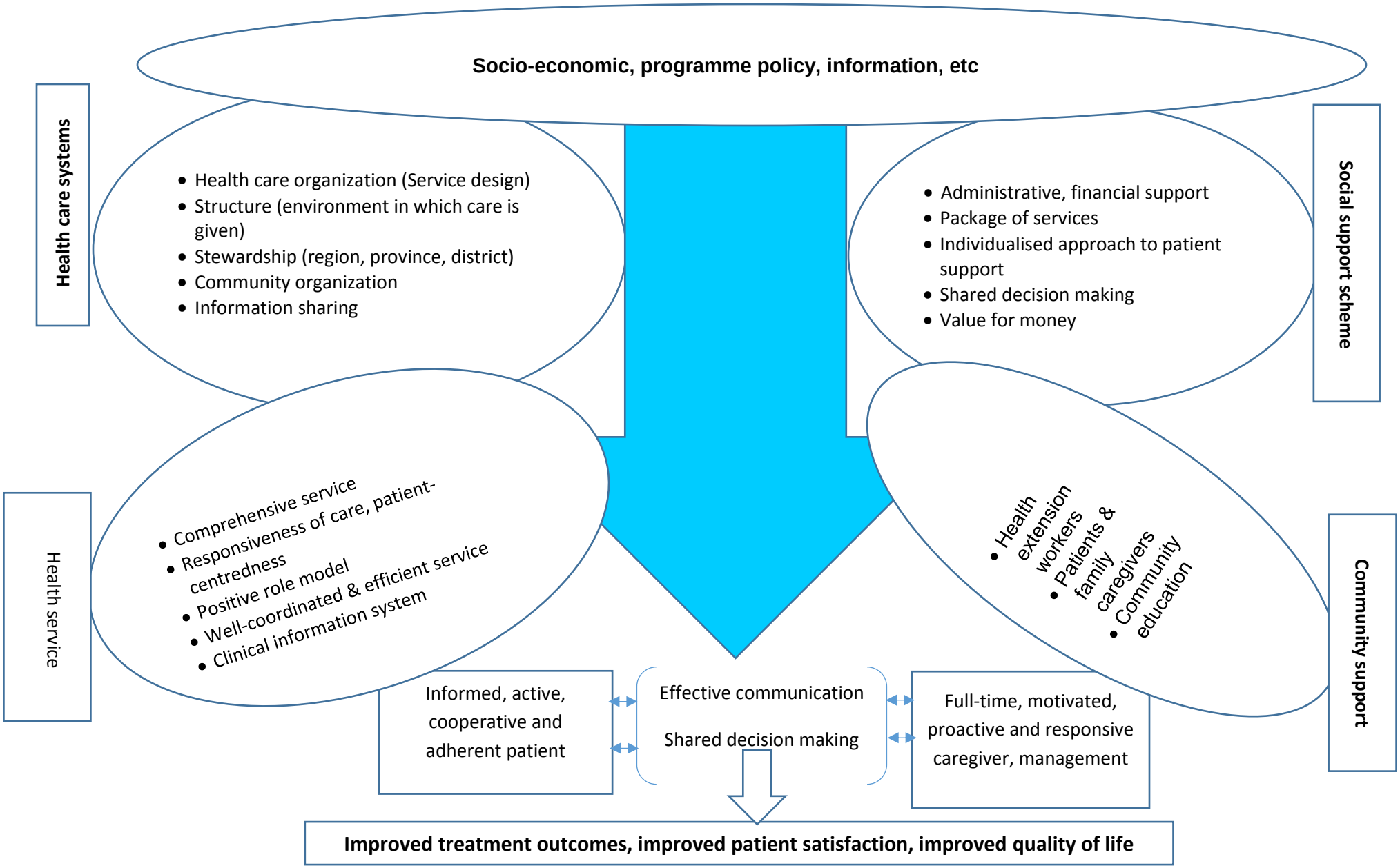


Figure 5. 1: A Conceptual model for enhancing the management of patients with MDR-TB in Ethiopia

5.5. Description of the components of the model and its practical application

A model cannot be understood in the absence of its components. As such, this section is devoted to describing the components of the model and its practical application to enhancing the management of patients with MDR-TB. In each section, two important issues are presented. First, a description of a component is presented. Second, the application of the component for enhancing the management of patients with MDR-TB is presented. The components of the model include the socio-economic, the community, the healthcare system and the patient and the careteam components (see figure 5.1). Implementation of the recommended activities for each component improves the management of patients with MDR-TB.

5.5.1. Socio-economic and programme policy component

In Ethiopia, the design for the management of patients with MDR-TB is a clinic based ambulatory model of care. Socio-economic support for patients with MDR-TB is a key component of the management of patients with MDR-TB (Federal Ministry of Health of Ethiopia 2014:16-17).

Yet, evidence from the current study demonstrates that patients with MDR-TB suffered from socio-economic problems associated with becoming a patient with MDR-TB. Patients with MDR-TB lost employment due to the disease. This was associated with the stigma associated with the disease and lack of the strength to continue jobs in the informal daily labour works. On the other hand, the available socio-economic support provided by the programme of MDR-TB was inadequate. Moreover, the system of delivery of the available socio-economic support was not patient-centred, as it is provided at the hospitals. To transport the nutrition items from the hospitals to their home areas, patients with MDR-TB incurred an unpaid cost of transportation. Moreover, there was weak system of check by the regional health bureau regarding the appropriate implementation of the patients' socio-economic support by the hospitals. Moreover, the financial reimbursement made by the programme to cover patients' transport costs, could not consider costs paid to local transport systems like the taxis, carts and the motor bikes on which patients could not present official receipts.

Furthermore, some patients linked to the community treatment follow up centres incurred cost to continue treatment. As the community health extension workers were not involved in providing daily treatment support for patients with MDR-TB, patients living in remote rural areas could not access their daily treatment within walking distances. Such patients were forced to rent houses in the towns of the treatment follow up centres in order to be close to the MDR-TB treatment follow up centres. Yet, there was no accommodation allowance for the remote rural patients linked to the treatment follow up centres.

5.5.1.1. Application to enhancing the management of patients with MDR-TB

There is national enabling policy platform for the application of the socio-economic component related recommendations of the model. The National Health Account shows that, in Ethiopia, health shares 5.2 percent of the gross domestic product which meets the 5% of gross domestic product recommended by the World Health Organization (Federal Ministry of Health 2014:16). There is regular flow of fund for the MDR-TB programme from the regional health bureau to the hospitals that are managing MDR-TB (Federal Ministry of Health of Ethiopia 2014:86).

In this regard, the programme policy component can facilitate decisions about patient care or the organization and delivery of the clinical and other services based on the needs and preferences of patients with MDR-TB. Moreover, actors in the programme policy component (policy-makers, managers, clinicians) have the capacity to facilitate implementation of the recommendations included in this model inline with programme priorities and the availability of resources.

To this end, the Oromia Regional Health Bureau need to revise the current approach to the socio-economic support provided for patients with MDR-TB. The support should address the needs and preferences of patients with the disease. The study revealed differing socio-economic support need by patients with differing social status. Thus, the current socio-economic support need to align with the socio-economic support need of a particular patient with MDR-TB than the current ‘one size fits all’ or uniform approach for all patients with MDR-TB.

Moreover, the mode of delivery of the nutrition support should be patient-centred, that is, the support (nutrition items) should be delivered as near to the patients' home area as possible.

Furtheremore, this model recognizes that the regional health bureau need to monitor the accountable and cost-effective use of available programme resources. Moreover, the regional health bureau need to address the invisible indirect cost incurred by the remote rural patients in their effort to continue treatment after linkage to the community treatment follow up centres, This can be done, through the decentralisation of the daily treatment service closer to the patient's home area, preferably through the active involvement of the health extension workers. To tackle the stigma associated with MDR-TB, the regional health bureau need to strengthen community education on MDR-TB. Moreover, the model is a reminder for the hospital level leadership to support the programme of MDR-TB through taking the lead responsibility to make sure that socio-economic support provided for patients with MDR-TB addresses the needs and preferences of patients with the disease. The hospitals' management should use the views and opinions of patients with MDR-TB and the views of the caregivers for MDR-TB in the planning and implementation of the socio-economic support given for patients with MDR-TB. Furthermore, the hospitals should disburse nutrition items closer to the patients' home area, or at least at the level of the community based treatment follow up centres for MDR-TB.

5.5.2. The community component

In Ethiopia, the community is part of the outpatient based ambulatory model of care for patients with MDR-TB. The community supports case finding and patients' treatment support at family level. The health extension workers, who are responsible for supporting patients with MDR-TB through daily treatment observation are found in the community. Health extension workers also lead the activity of community education and respiratory MDR-TB infection prevention at the community and household levels (Federal Ministry of Health of Ethiopia 2014:21).

However, this study revealed that there was no clear direction on the specific roles of the community in patient treatment support. Moreover, the health extension workers were not involved in the patient treatment support and respiratory MDR-TB infection prevention at the level of the community and patients' homes. The competencies of the health extension workers and patient families regarding treatment support, the issue of patient confidentiality and prevention of stigma was not known. The involvement of patient families in patient treatment support was erratic. Given the fact that a huge number of tablets of each of the second-line drugs are taken by an MDR-TB patient per day, no evidence on the quality of handling the second-line drugs at home and on the quality of daily drug provision under observation.

There was no practice of making sure that the patients' household conditions ensure the respiratory MDR-TB infection control requirements. Furthermore, there was no system of monitoring implementation of the nationally recommended community level interventions on MDR-TB. Because of lack of appropriate education to the community and the patients' families on MDR-TB, substantial proportion (6%) of the total patients included in this study were diagnosed among close contacts of the index patients with families.

5.5.2.1. Application to enhancing the management of patients with MDR-TB

The model has identified the gaps between the programme recommendations and the implementation of the recommended community level interventions on MDR-TB. As such, implementation of the model facilitates clarification of the specific roles for the health extension workers and the family treatment supporters. Moreover, it helps to devise a means of checking for the competencies of the health extension workers and families to implement community level activities on patient treatment support, prevention of stigma and MDR-TB infection prevention. Likewise, the model guide revision of the specific roles of the caregivers at the hospitals and the treatment follow up centres to monitor the implementation of community level activities on MDR-TB programme.

5.5.3. The healthcare system component

Based on the ambulatory model of care for patients with MDR-TB, arrangements are made whereby patients are initiated on treatment at hospitals and then linked to the health centres for continuation of treatment and follow ups (Federal Ministry of Health of Ethiopia 2014: 18-19). Patients' daily treatment support is arranged at the health centres or at the level of the community by the health extension workers or family members.

However, the result of this study demonstrated that the programme lacked practical decentralization of clinical follow ups and socio-economic support that patients need after linkage to the community. Patients were expected to attend a compulsory monthly visits to the hospitals to attend MDR-TB clinic days and also to get the socio-economic support disbursed at the hospitals. The views and opinion of the patients with MDR-TB was not used in the planning and implementation of the socio-economic support given for patients with MDR-TB. Thus, both patients with MDR-TB and their caregivers perceived that the socio-economic support, particularly the nutrition support received by patients, did not meet the needs and service preferences of patients with MDR-TB. Moreover, there was no strong monitoring mechanism from the Regional Health Bureau to make sure that patients with MDR-TB were actually getting the right package of the socio-economic support for which the patients were eligible.

At the hospitals, there was no physician dedicated for the MDR-TB treatment centre so that physicians were not readily accessible for patients' emergent medical conditions.

Furthermore, the MDR-TB treatment centre was not providing integrated service on MDR-TB and co-morbidities with it, especially co-infection with HIV/AIDS. The system was not tracking engagement of the health extension workers in patient treatment support and in MDR-TB infection prevention at the community level. Available programme support from the management of the hospitals and the general healthcare management was weak. At the hospital level, the setups in which care was given for patients with MDR-TB lacked cleanness and recreation facilities.

Additionally, most of the treatment follow up centres were not accessible to the majority of patients who live in the remote rural areas. As such, most patients linked to the community had to move away from their home area and dwell in the home town of the treatment follow up centres. This has caused financial consequences on patients as patients had to pay for house rent. This was a concealed financial grievance on the remote rural patients with MDR-TB.

5.5.3.1. Application to the programmatic management of patients with MDR-TB

The healthcare system related recommendations of the model can be implemented within the available programme platform and available resources. The hospitals need to revise the current approach to the clinical follow ups and socio-economic support given for patients with MDR-TB. Patients should get clinical follow-ups by a physician and the socio-economic support at the community based treatment follow up centres. This reduces the financial and time burden of patients who travel long distances to hospitals to get these services. The hospitals need to solicit the views and opinions of patients with MDR-TB in the planning and implementation of the socio-economic support available for patients with MDR-TB. At the hospitals, a physician dedicated only for the MDR-TB treatment centre; and who is 24 hours accessible for patients' emergent medical conditions should be assigned. At the MDR-TB treatment centre, integrated treatment and follow-up services should be available on MDR-TB and associated co-morbidities, particularily HIV/AIDS under one roof and by the same caregiver. The healthcare system should urgently engage the health extension workers on patient treatment support, respiratory MDR-TB infection prevention at household level and the reduction of stigma against patients with MDR-TB. For this, the healthcare system need to clarify the roles of each actor in the implementation

of community level interventions on MDR-TB. In cases when family members are considered to provide daily treatment support for patients with MDR-TB, the healthcare system should provide tablet bags to facilitate safe handling of the second-line drugs at the patients' homes. The managements at the hospitals, health centres and the general health system should be closely steering implementation of the continuum of care and services available for patients with MDR-TB.

5.5.4. The patient with MDR-TB and the healthcare team component

The approach in which the healthcare team provides care and services determine patients' satisfaction with the care given (Višnjić et al 2012:54). The meaningfulness of the evidence-informed practice is determined by the way in which it is experienced by the patient who uses the services. Thus, the outcomes of any health intervention is considered desirable if it reflects the patients' preferences rather than the caregivers' (Pearson, Field & Jordan 2007:20). In Ethiopia, the healthcare team for the MDR-TB programme is composed of a panel of experts with varying disciplines from the hospitals, the general health management and other stakeholders. The panel team is responsible for steering the clinical and non-clinical services given for patients with MDR-TB (Federal Ministry of Health of Ethiopia 2014:23).

In this study, it was noted that the prevailing approach to the management of patients with MDR-TB could not address the needs and preferences the patients with MDR-TB. Specifically stated, there was weak effort in the identification of the socio-economic, behavioural and motivational support needed by patients with MDR-TB. Patients were not active role players in the decisions made regarding the socio-economic support and the clinical care they receive on MDR-TB. There was no smooth communication and information sharing between patients and their caregivers, particularly at community level treatment follow up centres where patients could not get empathic and caring services. Moreover, the awareness of patients and their families on MDR-TB was very low. Thus, family caregivers were at risk of respiratory MDR-TB infection.

5.5.4.1. Application to the programmatic management of patients with MDR-TB

The healthcare team need to transform the current passive service recipient status of patients towards a fully informed and motivated patients who can share responsibility on the care they receive for MDR-TB. For this, collaborative communication should be strengthened between patients and their caregivers with emphasis to the treatment follow up centres. At treatment inception, the healthcare team need to identify the peculiar socio-economic and clinical support need of a patient with MDR-TB and tailor patient's supports towards his or her needs and preferences. The hospital management need to consider the recommendations of the healthcare team in planning clinical and socio-economic services for patients with MDR-TB. Furthermore, the healthcare team should strengthen community awareness on MDR-TB, prevention of respiratory MDR-TB infection and the stigma against patients with MDR-TB.

5.6. Strengths and limitations of the model

Implementation of the recommendations of this model are feasible as it can be implemented within the available programme context and the available programme resources. Moreover, the interventions in the model are meaningful for patients with MDR-TB as it addresses the values and the preferences of the patients who use the services given for MDR-TB. In summary, implementation of the model improves patients' satisfaction with care given for MDR-TB, patients' adherence to treatment and the treatment outcomes of patients treated for MDR-TB.

Therefore, the researcher believes that the model will have extensive use in guiding programmatic and clinical practice in the care of patients with MDR-TB. The model has incorporated important concepts that are known to determine the process and the outcomes of patients treated for MDR-TB and patients' satisfaction with care given for MDR-TB. The multiple concepts incorporated into the model have the potential to serve as a reference for caregivers on MDR-TB. The model will also guide coordination among main programme actors in the health system. As such, the model will aid decision making technically and programmatically. Therefore, the researcher believes that this model will have a multi-attribute additive value for improving the clinical and programmatic management of patients with MDR-TB. The researcher also believes that the model will

guide policy makers in the development of a patient-centred approach to the management of patients with MDR-TB. Hence, the model will highly improve treatment outcomes of patients with MDR-TB. It will also improve patient satisfaction with the care and services given for MDR-TB.

However, development of the model is based on data from two treatment centres. The programmatic context at the two centres may be different from the context of other centres. This may limit application of the model beyond the context of the treatment centres included in this study.

5.7. Summary

Chapter five presented discussions on model development. The term model was defined and its uses were described on a conceptual basis for representing how a programme was supposed to work. The strategy used for the development of a model was discussed. The chapter also discussed the various sources of data for the development of the model for enhancing the treatment for patients with MDR-TB. Ultimately, the chapter presented the components of the model developed and the application of each component in enhancing the programmatic management of patients with MDR-TB. The next chapter, chapter 6, presented a detailed discussion on the major results of the study.

Chapter 6: Discussions

6.1. Introduction

The results of this study were presented in the previous chapters. This chapter presents the discussions of the results in line with the available literature. In this chapter quantitative and qualitative results are discussed together. Moreover, implications of the results of this study on the current practice in the clinical and programmatic management of MDR-TB in the Oromia Region of Ethiopia are shown.

6.2. Discussions on key results

6.2.1. Treatment outcomes of patients treated for MDR-TB

6.2.1.1. Interim treatment outcomes

This study revealed that at six month after commencing treatment, 71% of the patients were culture negative. Yet, 20% of the patients were died of MDR-TB by month six. The 71% culture negative rate by the end of six month revealed in this study is more than the 62% rate of culture conversion reported among patients treated at treatment centres in Amhara and Oromia Regions of Ethiopia. But the 27 (20%) death rate revealed in this study is more than 10% reported among the same (Molla, Jerene, Jemal, Nigussie, Kebede, Kassie, Hiruy, Aschale, Habte, Gashu, Kebede, Melese & Suarez 2017: 31).

The result of this study is consistent with the study conducted in South Africa in which it was found that, compared with the HIV negative patients with MDR-TB, HIV positive patients with MDR-TB had a lower chance of culture conversion and a higher chance of death (35.2% deaths among HIV positive patients with MDR-TB was compared to the 16.2% death among HIV negative patients with MDR-TB, P-value<0.0001) (Lange et al 2014:47).

6.2.1.2. Final treatment outcomes of patients with MDR-TB

This study revealed a composite treatment success rate of 69% and a death rate of 30 (27) % among patients with MDR-TB included in the study. The 69% treatment success rate is less and the 27% death rate is higher respectively than the 75% treatment success rate and the 15% death rate reported respectively by Molla et al (2017:31). Moreover, this level of treatment outcome is lower than the composite treatments success rate of 78.6% reported by Meressa et al (2015:1181). On the other hand, the 69% treatment success rate revealed in this study is similar to the 70.6% treatment success rate reported by Anderson et al (2014:406) Moreover, the 1% rate of lost to follow ups revealed in this study is less than both the 5.9% reported by Meressa et al (2015:1183) and the 8% lost to follow ups reported by Molla et al (2017:31).

According to the report by Anderson et al (2013:406), HIV co-infection with MDR-TB is associated with a higher rate of default from treatment and death from MDR-TB. In the view of the report by Anderson et al (2013:406), the relatively low treatment success rate revealed in this study compared to the report by Meressa et al (2015:1181), might be due to the higher proportion of any co-morbidity (31%) with MDR-TB at baseline and higher MDR-TB and HIV/AIDS co-infection (25%) among patients included in this study. Moreover, the intensive nutrition support and the intensive management of adverse drug reactions from second-line drugs through the direct support of a non-governmental organization collaborating with the Ministry of Health as reported by Meressa et al (2015:1183), was not comparable with the desperate nutrition support reported by patient with MDR-TB and their caregivers included in this study. Such differences might also explain the lower treatment success rate among patients with MDR-TB included in this study. Despite the high MDR-TB and HIV co-infection rate revealed in this study, the 1% lost to follow ups is presumably encouraging.

In Georgia, low monthly household income and unemployment were predictors of poor treatment outcomes among patients treated for MDR-TB (Djibuti, Mirvelashvili, Makharashvili & Magee 2014:1). In this view, the higher proportion of unemployement (35%) and employement in the informal labour works (53%), revealed in this study, might explain the higher rate of death among patients included in this study.

6.2.2. Determinants of the treatment outcomes of patients with MDR-TB

6.2.2.1. Socio-demographic and socio-economic characteristics and the treatment outcomes of patients with MDR-TB

The study revealed that 94% of the patients included in the study were in the productive age group of 15-64 years. It is worth noting that 93% of the total deaths from MDR-TB was also occurred in the same age group. Moreover, the study revealed that only 5% of the study participants were employed in the formal sector. Thirty five percent of the patients were not employed and 53% were self-employed in the informal sector; which shows the low socio-economic status of patients with MDR-TB included in this study.

On the other hand, the interviews conducted with patients with MDR-TB revealed that, the 53% self-employment was described as employment in the informal labour workforce with minimum daily wages. It was also revealed that, some patients lost job and income as a result of failing to engage in their usual business activities like the labour work, which needs physical strength. Sixteen out of the total 18 patients with MDR-TB who participated in the interviews with patients did not have any means of getting an income. Such patients depended on the socio-economic support provided through the programme of MDR-TB. However, the socio-economic support obtained from the programme was reported to be inadequate. The nutrition support provided by the programme is not adequate both in terms of its quantity and quality.

Termination of job due to MDR-TB and its treatment has caused multiple challenges on patients with the disease. Patient participants of the interviews associated poverty with the occurrence of MDR-TB. Some participants believed that poor economic status and the poor quality of food that they used to eat have put them at risk of contracting the MDR-TB disease. Participants also experienced that poverty challenges patients' ability to adhere to the lengthy treatment given for MDR-TB. The disease hampered patients' ability to cope up with both the disease and the treatment given for it. For example, the poor rural patients could not afford the daily indirect expenses incurred to attend to the daily treatment at the treatment follow up centres. Moreover, participants perceived that MDR-TB becomes more severe among the poor patients who could not get adequate food, in which the disease was described that it easily collapses patients with poor nutrition status.

On the other hand, the nutrition and financial support provided for patients by the programme of MDR-TB was revealed to be inadequate. The study revealed that most patients with MDR-TB depend on the income of their families. This helps when the patient with MDR-TB has a family with a monthly income. However, the qualitative inquiry revealed that families of most of the patients with MDR-TB did not have monthly income and live on subsistence income.

Furthermore, some of the patients with MDR-TB are bread winners for their family and have dependents to take care of. Patients with MDR-TB who had dependents but no income to take care of their dependents were obliged to share the food (nutrition) they got from the MDR-TB programme with their dependents. Such patients expressed the desperate condition associated with becoming a patient with MDR-TB. Such patients bitterly expressed the difficulty of taking the multiple drugs given for MDR-TB in the absence of adequate food to eat daily. Patients claimed that the MDR-TB disease aggravated the already poor living condition they had.

On the other hand, patients with MDR-TB faced stigma that separated them from their family members and from continuing the usual daily labour work in which they were employed before. Moreover, the stigma was reported to have resulted in the termination of employment including by those who were professionally employed. As such, patients could not continue with their usual social roles once they were diagnosed with MDR-TB and started on treatment. This resulted in the worsening of the patients' economic status that affects not only the patients themselves but also their dependents and families.

As such, this study revealed that low socio-economic status and the inadequate socio-economic support that patients received through the programme of MDR-TB has challenged patients' coping ability to the challenges associated with being a patient with MDR-TB. The study revealed that patients with MDR-TB faced multiple adverse outcomes from MDR-TB. On the top of the body ailments from the disease, patents with this disease faced economic or financial problems, social problems like stigma, psychosocial problems including the discontinuation of employment.

The result of this study reminds us the theory of fundamental causes of disease. The theory of fundamental cause states that social and economic conditions are fundamental causes of inequalities in health and disease. According to the theory of fundamental cause, the use of resources to benefit health, by groups and individuals, is purposeful. Thus, the health advantage of high socioeconomic status is not a coincidental. The theory argues that the deliberate use of resources by individuals and groups to benefit health is essential in producing the enduring association between socioeconomic status and disease and mortality (Phelan, Link, Diez-Roux, Kawachi & Levin 2004:268-70).

According to the theory of fundamental cause, social conditions influence multiple disease outcomes, meaning that it is not limited to one or a few disease or health problems. Second, it affects these disease outcomes through multiple risk factors. Third, the association between the fundamental cause and health is reproduced overtime via the replacement of the intervening mechanisms. Fourth, the essential feature of the fundamental social causes is that it involves access to resources that can be used to avoid risk factors or minimise the consequences of a disease once it occurs. In this way, the theory states that, individuals with low socio-economic status lack resources like money, knowledge, prestige, power and beneficial social connections that protect health irrespective of what mechanism is available to combat the adverse outcomes of a given disease entity (Phelan, Link & Tehranifar. 2010: S29-30). In this study, poverty and the lack of adequate food was perceived by patients as a precursor for their catching the disease, MDR-TB. Once dignosed with the disease, patients with MDR-TB encountered worsening socio-economic and psychosocial problems including lost jobs and stigma associated with the disease.

The result of this study is consistent with the report by Dheda et al (2014:342) and the report by Djibuti et al (2014:1). These reports indicated that low monthly household income, living in poverty and unemployment are predictors of poor treatment outcomes among patients with MDR-TB. In view of these reports, the high rate of unemployment revealed among patients with MDR-TB included in this study, seems to be a potential challenge for patients with MDR-TB to adhere to the standard schedule of the treatment given for MDR-TB. Moreover, the result of this study is consistent with the report of the World Health Organization which states that patients with tuberculosis are too weak to continue working so that their families are obliged to pay for the expenses needed for care seeking.

Acknowledging this, patients with MDR-TB suffer direct costs that they incur in seeking care for the disease and indirect costs as a result of lost jobs due to the disease (WHO 2013b:7). The qualitative interviews also revealed that there were patients who noted that they were infected with MDR-TB because of the lack of adequate food. Moreover, patients perceived that lack of adequate food has challenged their coping ability with the treatment. This result is consistent with the report that MDR-TB imposes socio-economic problems on patients affected by the disease. In the presence of free treatment for MDR-TB, patients incur indirect costs through income loss due to the disease. As such, reduced monthly income due to unemployment is a predictor of poor treatment outcome among patients with MDR-TB (Djibuti, Mirvelashvili, Makharashvili & Magee 2014:1).

The stigma and discrimination on patients with MDR-TB, revealed in this study, is consistent with the report of Cremers et al (2015:2) in which 82% of patients with tuberculosis in Urban Zambia encountered some form of stigma due to tuberculosis. In Sudan, stigma due to tuberculosis was higher among the unemployed and the rural patients (Suleiman et al 2013: 390-92). In this view, the higher proportion of unemployment among patients included in this study might contribute to the experience of stigma reported by the patients included in this study.

6.2.2.2. Clinical characteristics and treatment outcomes of patients with MDR-TB

This study has shown a composite treatment success rate of 69%. Moreover, it revealed a 27% death rate from MDR-TB by the end of month 24. One of the clinical factor that was associated with the treatment outcomes of the patients was co-morbidity with MDR-TB. Forty one (31%) of the patients with MDR-TB had some form of co-morbidity with MDR-TB at the baseline. From the total, co-morbidity with MDR-TB at baseline, 34 (83%) was due to co-infection with HIV while 5 (12%) was due to co-infection with diabetes mellitus. The treatment success rate among patients included in this study was lower than the 78.6% treatment success rate reported among patients treated at Gondar Health Science Hospital and the St Peter's Hospital in Addis Ababa. Moreover, the 31% of co-morbidity with MDR-TB at the baseline and the 26% rate of MDR-TB co-infection with HIV are higher than the 21.7% reported among patients with MDR-TB in Ethiopia. Likewise, the 27 % death rate is

more than the 13.9 % death rate reported among the same patients (Meressa et al 2015:1181).

This study revealed that the presence of any co-morbidity with MDR-TB at the baseline is significantly associated with the occurrence of death among patients with MDR-TB (AOR=4.260, 95%CI: 1.607-11.29; p<0.004). This result is consistent with the study conducted in the United Kingdom (Anderson et al 2013:406), in which it was cited that the presence of any co-morbidity with MDR-TB at the baseline is a risk factor for death (p<0.0005). Moreover, this result is consistent with the reports of Gandhi et al (2012:90) and Babatunde et al (2013:213), in which it was cited that immunosuppression among MDR-TB and HIV-co-infected patients is associated with poor treatment outcomes and high mortality among patients treated for MDR-TB.

6.2.2.3. Malnutrition and the treatment outcomes of patients with MDR-TB

The study revealed that 64% of the patients included in this study had a body mass index (BMI) of less than <18.5kg/m^2, which is indicative of malnutrition associated with MDR-TB. This study revealed that the low body mass index (BMI), is significantly associated with unfavourable treatment outcomes of patients with MDR-TB (AOR=2.734, 95%CI: 1.01-7.395; P<0.048). It is cited in the literature that pre-existing malnutrition among patients with MDR-TB and the lack of proper nutrition in the course of patients' treatment affects patients' response to treatment and hampers recovery which in turn results in poor treatment outcomes among patients with MDR-TB (Caminero 2013:201).

As such, the result of this study commensurate with the report by the World Health Organization (WHO) (2013b:8), that low Body Mass Index (BMI) and lack of adequate weight gain is associated with death and relapse of tuberculosis. Moreover, a low body mass index (MBI<18.5kg/m^2) increases the chance of occurrence of adverse drug reactions from second-line drugs. Thus, the 64% prevalence of malnutrition among patients included in this study is an indication of disease severity and poor patient response to treatment. The association between malnutrition and unfavourable treatment outcomes revealed in this study is also consistent with other studies. It was reported by Yuan et al (2013:1) that malnutrition is an established risk factor for poor treatment outcomes among patients with MDR-TB. Moreover, the result is consistent with the report by Vishakha and Sanjay

(2013:57), in which it was cited that malnutrition with MDR-TB is associated with a low cure rate and a high rate of death among the poor patients with MDR-TB in Ahmedabad. Thus, addressing malnutrition presenting with tuberculosis is crucial for improving patient response to tuberculosis treatment (Whitney et al 2008:197).

6.2.2.4. Status of the availability of integrated care for MDR-TB and HIV co-infected patients

The interviews held with caregivers in the qualitative component of this study has revealed that despite the high level of MDR-TB and HIV/AIDS co-infection rate among patients included in this study, the current programme of MDR-TB is not providing services for MDR-TB and HIV/AIDS under one roof and by the same caregiver. Information on the management of HIV for co-infected patients were not available at the MDR-TB treatment centre. Therefore, data on MDR-TB and HIV/AIDS co-management, if any, is obtained only from the patients' verbal reports. First, caregivers practicing at the MDR-TB treatment centre did not have the training on the treatment of HIV/AIDS so that they could not prescribe anti-retroviral drugs (ART). Second, the MDR-TB treatment centres do not handle anti-retroviral drugs. Thus the management of MDR-TB and HIV co-infected patients entails the involvement of different caregivers from different health facilities, departments or settings. In this way, the MDR-TB and HIV/AIDS co-infected patients were obliged to visit different caregivers in different settings to get care and services for both diseases.

The study revealed that none of the HIV and MDR-TB co-infected patients had documented T–lymphocyte cell bearing (CD4) count at the initiation of treatment for MDR-TB. As revealed by the interviews with caregivers, the absence of optimum care for patients co-infected with HIV might be due to the fact that HIV/AIDS related services were not provided in the same centre as the MDR-TB treatment centres.

The report by Babatunde et al (2013:213) and Tadesse (2015:65) indicated that the presence of co-infection with HIV is associated with poor MDR-TB treatment outcomes. In view of these reports, the absence of full information on the management of HIV/AIDS for patients infected by both MDR-TB and HIV/AIDS, revealed in this study, may explain the poor treatment outcomes of the HIV co-infected patients with MDR-TB.

As reported by Tadolini et al (2012:102-103) and the WHO (2010:15-16), globally, universal access to patient-centred treatment and care, is recommended for patients affected by the dual burden of HIV and MDR-TB. In view of these reports, the absence of integrated care under one roof that is provided by the same caregiver for patients affected by both diseases, as revealed in this study, indicates that the programme is not addressing the patients' right to patient-centred treatment and care on HIV/AIDS and MDR-TB and the protection of populations affected by both MDR-TB and HIV/AIDS.

Both MDR-TB and HIV/AIDS are chronic illnesses. They need regular clinical and laboratory follow ups. Thus, in the absence of an integrated care and follow up services for both diseases, co-infected patients face difficulty to comply with attending the treatment and the follow up care needed for both diseases as they visit different caregivers at different facilities. When they are enrolled to the treatment for MDR-TB, the routine follow up services that patients need for the HIV are not continued as usual. The reasons include that patients usually focus on the MDR-TB disease and the challenges of coping with taking the multiple second-line drugs daily and the associated adverse drug reactions. As such, patients usually revert their attention from the HIV/AIDS to the new problem of MDR-TB. Thus, there were incidences of anti-retroviral treatment failure and repeated incidences of sudden patient death among patients with MDR-TB who were co-infected with HIV/AIDS. Added to this, participants reported that patients do not often have the physical strength to visit different facilities to adhere to the prescribed treatment and follow up schedules of both diseases.

In summary, the absence of integrated care on HIV/AIDS and MDR-TB have created a lot of inconveniences on patients. Moreover, the caregivers for MDR-TB who participated in the in-depth interviews claimed that patients with MDR-TB are infectious to others especially to people living with HIV and those visiting the anti-retroviral therapy (ART) clinic. Caregivers reported that patients with MDR-TB and HIV who visit different centres to get services on HIV/AIDS and MDR-TB put the community at risk of respiratory infection with MDR-TB.

Furthermore, Ethiopia is one of the high burden countries for MDR-TB and HIV/AIDS co-infections (Falzon, Jaramillo, Wares, Zignol, Floyed & Raviglione 2013:690). Therefore, the absence of integrated services and care for MDR-TB and HIVAIDS under one roof was found to be associated with patients' dissatisfaction with the care given for MDR-TB. It also hampers patients' coping ability to attend to the separately located treatment and follow up requirements of both diseases. Therefore, the absence of integrated service for both MDR-TB and HIV/AIDS will continue to challenge the subsequent national effort in the prevention and control of drug-resistant tuberculosis in Ethiopia.

6.2.2.5. Status of the drug-susceptibility test (DST) service for patients with MDR-TB

The majority (99%) of the patients with MDR-TB included in this study had drug-susceptibility test done only for rifampicin. Fifty eight (43%) of the patients had documented drug-susceptibility test result for both rifampicin and isoniazid. For the rest of first and the second line anti-tuberculosis drugs, drug-susceptibility test result status of the patients with MDR-TB was unknown. This indicated that the status of the drug-susceptibility test service that patients obtained through the programme was limited. Scholars cited that limited availability of drug-susceptibility test services for patients with MDR-TB leads to the use of inappropriate regimens. In turn, the use of inappropriate regimens leads to the further amplification of resistance (Dobler et al 2015:1451). In the view of such recommendations, the current status of the drug-susceptibility test services available for the patients with MDR-TB included in this study seems to be sub-optimal.

6.2.2.6. Adverse drug-reactions and the treatment outcomes of patients with MDR-TB

In this study all the patients with MDR-TB for whom data on adverse drug reactions from second-line drugs was available, experienced at least one episode of a form of adverse drug reactions in the course of their treatment for MDR-TB. The magnitude of occurrence of the adverse drug-reactions from second-line drugs ranged from the minimum of one episode to five episodes per patient.

The magnitude of adverse drug reactions revealed in this study is higher than the overall 78% and the median of three adverse drug reaction events per patient reported by Bloss et al (2010:275). Moreover, this rate of adverse drug reactions among patients included in this study is higher than the 71.7% reported by Akshata et al (2015:28) and also more than the 57.14% prevalence of adverse drug reactions reported by Vishakha and Sanjay (2013:55). But the prevalence of adverse drug reactions among patients with MDR-TB included in this study is similar to the 72/73 (99%) rates of adverse drug reactions reported by Bezu et al (2014:147) among patients treated at government health centres in Addis Ababa, Ethiopia.

According to the report of the World Health Organization (WHO 2014b:85; WHO 2012b:65) and that of Caminero (2013:172), the presence of co-morbidities with MDR-TB that demand the simultaneous use of several drugs and presence of malnutrition with MDR-TB (WHO 2013b:7) are risk factors for the occurrence of adverse drug reactions. In this view, the high proportion of co-morbidity with MDR-TB including malnutrition with MDR-TB, revealed in this study, might explain the occurrence of adverse drug reactions among patients included in this study.

Analysis of the trend of occurrence of adverse drug reactions showed that the majority of the adverse events occurred during the injection based initial months of the intensive phase of MDR-TB treatment. The study revealed that except in the case of ototoxicity and musculo-skeletal and neurological adverse drug reactions, the occurrence of adverse drug reactions from second-line drugs decreased after the first six months of patient treatment. The decreasing trend in the occurrence of most of the adverse drug reactions from second-line drugs revealed in this study is consistent with the trend reported by Bloss et al (2010:277). This result signifies the need for intensive management of adverse drug

reactions and close patient management during the initial intensive phase months of the management of MDR-TB.

The qualitative inquiry revealed that the management of adverse drug reactions from second-line drugs was not adequate, on which patients were dissatisfied. The reasons described by patients with MDR-TB included absence of prompt treatment of adverse drug reactions when patients face the problem. Patients faced adverse drug reactions at any point in time in the course of their treatment be it at the hospital or at the treatment follow up centres. At hospital level, physicians were not reliably available for managing patients' emergent medical conditions from adverse drug reactions, especially during times out of the normal working hours.

Patients linked to the treatment follow up centres usually came back to the hospitals due to adverse drug reactions. In such cases, there were incidents when patients could not get immediate medical attention once they arrived at the hospitals. This was mainly associated with the absence of physicians dedicated 24 hours of the day for the MDR-TB treatment centre.

Caregivers for patients with MDR-TB mentioned multiple factors challenging the optimum management of adverse drug reactions from second-line drugs. These included absence of dedicated and reliable laboratory service to promptly diagnose adverse drug reactions related complications. This impedes caregivers' ability to timely diagnosis of adverse drug reactions. Moreover, caregivers at the hospitals felt that the caregivers at the treatment follow up centres lack adequate clinical skills to timely identify adverse drug reactions and refer patients back to the hospitals. There were also insufficient ancillary drugs that are required to treat the adverse drug reactions from second line drugs.

Available literature states that some of the severe adverse drug reactions like hypokalaemia and electrolyte wasting including hypoglycemia are common among patients treated for MDR-TB, particularly among those co-infected with HIV. Hypokalaemia results from both the anti-tuberculosis and anti-retroviral drugs. In this group of patients, renal insufficiency may occur due to repeated vomiting and dehydration resulting in lethal outcomes (Caminero 2013:141; Caminero 2010:624). In line with the reports of these scholars, the

high prevalence of adverse drug reactions revealed in this study is a potential risk factor for unfavourable treatment outcomes among patients with MDR-TB. Moreover, the absence of dedicated and reliable laboratory for the MDR-TB treatment centre challenges early diagnosis and prompt management of the adverse drug reactions among patients included in this study.

6.2.2.7. Status of the socio-economic support provided by the programme of MDR-TB for patients with MDR-TB

The study revealed that, the social and financial support provided by the programme of MDR-TB in terms of nutrition and financial support was inadequate. The condition was reported to be serious especially for patients who do not have relatives to support them. The nutrition provided was not sufficient both for patients treated as inpatients at the hospitals and those patients treated as outpatient at the treatment follow up centres.

On the other hand, significant proportion (35%) of the patients included in this study were not employed while 53% were employed in the informal sector like the daily labour work. Moreover, the qualitative inquiry revealed that most patients lost jobs to the disease which further aggravated their poor economic status. Futhreomore, some patients had family dependents to take care of. As such, it was shown that patients with MDR-TB who had dependents but no income to take care of their dependents were obliged to share the food (nutrition) they got from the MDR-TB programme with their dependents. For such patients, being a patient with MDR-TB created a desperate condition.

It was repeatedly cited that lack of adequate food for patients with MDR-TB is an established risk factor for unfavourable treatment outcomes among patients with MDR-TB (Heemskerk et al 2015:9). In this study 64% of the patients had low body mass index, which was indicative of malnutrition with MDR-TB. According to Caminero (2013:201), pre-existing malnutrition among patients with MDR-TB and the lack of proper nutrition in the course of patients' treatment affects patients' response to treatment and hampers recovery which in turn results in poor treatment outcomes among patients treated for MDR-TB.

As such, the high prevalence of malnutrition and the inadequate nutrition support for patients included in this study is an urgent problem needing immediate attention by the programme of MDR-TB. Firstly, the nutrition support was quantitatively inadequate.

Second, it is disbursed at the hospitals which is very far from the residence area of most patients. So that patients incurred an unnoticed cost to transport nutrition items from the hospitals to their home.

Moreover, the financial support provided by the programme to cover the cost of transport was revealed to be inadequate. Participants mentioned that the financial support considers only the round trip costs paid for the intercity transport fees paid for buses between the patients' hometown and the hometown of the hospital treatment initiating centres. Financial support does not consider the transport fees that patients pay between their home areas to the formal bus stations using carts and motorcycles. Patients who are linked to the community based MDR-TB treatment follow up centres and who live far away from the treatment follow up centres also face difficulty in attending the daily observed treatment schedule arranged at the health centres. This is because, there was no housing allowance or accommodation arrangements for patients living far away from the MDR-TB treatment follow up centres. Thus, such patients were forced to pay for accommodation in the hometown of the MDR-TB treatment follow up centres.

In summary, poverty or the low socio-economic status of patients and their family caregivers is a challenge for both the latter and former. Poverty aggravates the challenges associated with being a patient with MDR-TB. Therefore, for the success of the programmatic management of MDR-TB in the Oromia Region of Ethiopia, the programme needs to address the socio-economic challenges that patients with MDR-TB face equally as treating the MDR-TB disease. In the context of this study setting, patients treated for MDR-TB need, at least, adequate social support in terms of nutrition and financial support. This can potentially improve patients' adherence to the standard treatment schedule for MDR-TB and the treatment outcomes of patients treated for MDR-TB.

6.2.2.8. Patients' adherence to the treatment given for MDR-TB and status of decentralization of the MDR-TB treatment to the community

In this study, 87.1% of all the patients with MDR-TB enrolled to treatment had an optimum level of adherence to the treatment given for MDR-TB. For the rest of the patient's, adherence to the lengthy treatment was noted with evidence of missed daily drug doses. In this study, all the 91 patients assessed for adverse drug reactions experienced at least one episode of adverse reaction from second-line drugs and also, 41 (31%) of the patients had some form of co-morbidity with MDR-TB at baseline. Given this fact, the 87.1% rate of adherence revealed in this study was encouraging. This level of patients' adherence is better than the 60% non-adherence reported by Robinson et al (2010:87). It is also more than the 50% non-adherence reported by Bosworth et al (2006:147).

However, the level of adherence revealed in this study is lower than the recommendation of the World Health Organisation which recommends that patients' non-adherence to standard tuberculosis treatment, should not exceed 5%. The World Health Organisation stresses that patient's adherence to treatment plays a key role in achieving optimum treatment outcomes and in the prevention of drug resistant tuberculosis (HerreroI et al 2015:288).

In this study various factors were implicated in patients' failure to strictly adhere to the standard treatment given for MDR-TB. This included, the social and financial hardships associated with inadequate income and lost income due to the disease, MDR-TB. In this study over half (53%) of patients with MDR-TB were employed in the informal sector. Such employment was described by patients to be mainly in labour work with minimum daily wages. Moreover, 35% of the patients with MDR-TB were not employed and were found to live on income from their family members. Such socio-economic difficulties put patients into difficulties to adhere to the lengthy treatment schedule for MDR-TB. This result is consistent with the report by Arakawa et al (2011:1000) in which it was cited that poverty and its associated factors impede patients' adherence to tuberculosis treatment. In this way, failure of patients to strictly adhere to the treatment given for MDR-TB due to social and economic constrains and absence of social protection contributes to poor treatment outcomes and further transmission of drug-resistant tuberculosis (WHO 2014b:10-11).

This study revealed that, for most patients, the daily observed treatment support was not easily accessible after patients are linked to treatment follow up centres. The reason was that, the health extension workers who are living in the community were not engaged in the provision of daily treatment support for patients with MDR-TB at the patients' nearby home area. Therefore, patients with MDR-TB were forced to attend the daily observed treatment at treatment follow up centres, which were far from the patient's village. This is a difficult situation for the patients who live in remote rural areas and who cannot afford accommodation fees to live in the hometown of the treatment follow up centres. This difficulty negatively impacts on patients' adherence to the lengthy treatment given for MDR-TB. Some of the caregivers for MDR-TB mentioned that, for some patients who live far from the treatment follow up centres, a one week dose of the second-line drug is given to the patients' homes. However, given the fact that a huge number of tablets of each of the second-line drugs are taken by an MDR-TB patient per day, no convincing practice was mentioned on the quality in which the second-line drugs were handled at the patients' homes.

This result is similar to the report by HerreroI et al (2015:295) in which the absence of strong community level treatment support was cited to be associated with patient non-adherence to treatment. Moreover, the result is consistent with the report by Alobu et al (2014:782-3) that in tuberculosis high burden countries such as Ethiopia, Indonesia, Pakistan and Nigeria, service inaccessibility to the remote rural patients is associated with poor adherence to treatment and a high death rate from tuberculosis. The study also revealed that patient's perception of high disease severity was found to hamper adherence to treatment. Due to hopelessness, perception of high disease severity affects patients' adherence to the treatment for MDR-TB. For example, some patients who faced severe adverse drug reactions mentioned that they lost hope of being cured by taking the drugs, which are toxic. This result is consistent with the report by Bosworth et al (2006:249) in which the perception of high disease severity is a factor associated with non-adherence to treatment perhaps due to pessimism about the ability of the treatment to alter the outcome of a serious illness.

6.2.2.9. Follow up laboratory services for patients with MDR-TB

This study revealed that the usage of laboratory services available for patients with MDR-TB is sub-optimal in the study areas. It is revealed that only 15% of patients with MDR-TB had satisfactory levels of access to routine follow up laboratory services in the course of their treatment for MDR-TB. For the 85% of the patients access to follow up services was limited to only very few of the WHO recommended and nationally adopted standard laboratory follow up services. As such, the observed level of available follow up laboratory services, indicates that the programme was not providing the standard follow up laboratory services recommended by the WHO for follow up of patients with MDR-TB while on treatment (WHO 2014b:146). Caregivers who participated on the in-depth interviews mentioned that it made it difficult for them to recognize and promptly treat some of the life threatening adverse drug reactions that could only be known only through routine laboratory tests.

The qualitative interviews with care givers also revealed that the MDR-TB centres lacked dedicated laboratories to provide follow up services for patients with MDR-TB. Moreover, available general hospital laboratory services lacked the key laboratory test services needed for the patients with MDR-TB. For example, the laboratories lacked the basic laboratory reagents needed to perform hormonal and electrolyte tests which are essential for patients on treatment. Caregivers reported incidences of apparent clinical signs of severe adverse drug reactions from second-line drugs like the hypokalemic tetani that could have been prevented if an adequate follow up laboratory services were available for the MDR-TB centre. Caregivers perceived that some of the sudden patient deaths observed during treatment might be due to drug adverse reactions that could have been prevented or promptly diagnosed through close laboratory follow ups.

As such, the result of this study revealed that in the current study area, follow up services through laboratory tests for which patients with MDR-TB were eligible were not available according to the national programme guideline (Federal Ministry of Health of Ethiopia 2014:119-131). Thus, patients were not getting the minimum package of the routine follow up laboratory services nationally recommended for follow up of patients with MDR-TB while

on treatment (Federal Ministry of Health of Ethiopia 2014:76). On the other hand, it is well documented that severe adverse drug reactions like hypokalemia and electrolyte wasting are common, especially among MDR-TB and HIV co-infected patients who are treated for both diseases. These adverse drug reactions increase the risk of renal insufficiency leading to lethal outcomes among patients with MDR-TB co-infected with HIV (Caminero 2013:141). Thus, it seems very difficult for caregivers in the study area to diagnosis and promptly treat some of the life threatening adverse drug reactions from second-line drugs that are diagnosed only through routine laboratory follow ups.

6.2.3. Patients' perceived quality of care and their satisfaction with the care given for MDR-TB

The study revealed that, patients with MDR-TB were satisfied with the clinical care that they received from caregivers found at the hospitals. Hospital level caregivers were described as empathic and caring. But at hospitals, patients were dissatisfied with the absence of a reliable care by a physician during patients' emergent medical conditions. Moreover, patients with MDR-TB were dissatisfied with the poor quality, inadequate quantity and the mode of delivery of the nutritional support they received from the hospitals and with the absence of patient involvement in nutrition related decision making process. Similarly, patients were dissatisfied with the amount of financial support they received and with the lack of recreation facilities within the premises of the hospital MDR-TB treatment centres and also with the lack of cleanness of the utilities found in the MDR-TB treatment centres. On the other hand, patients with MDR-TB were dissatisfied with the clinical care that they received from the caregivers found at the community level MDR-TB treatment and follow up centres. The patients experienced that caregivers found at the treatment follow up centres were not empathic and caring. Caregivers found at the treatment follow up centres were described, by patients, as non-communicative and alienating. Thus, patients with MDR-TB felt desperate, vulnerable and alienated, a situation revealed to determine patients' perceived quality of care and their satisfaction with the care given for MDR-TB.

According to the philosophy and science of caring, one's own philosophy and value system affects the encounters, relationships and the moments we have with ourselves and others. Emotions of love, kindness, gentleness, compassion, equanimity, and so on are intrinsic to

all humans. These emotions and experiences are the essence of what makes us human and deepens our humanity and connection with human spirit. This awareness gives us the energy to live beyond our individual ego-self and reminds us that we belong to the universe of humanity. For patients with MDR-TB, hospitalization and the challenges associated with taking the treatment given for the disease, is an event that can lead patients to a loss of human dignity (Watson 2008:42-3). Thus, it is the responsibility of the healthcare givers to help maintain and restore that dignity among patients treated for MDR-TB.

In the efforts made to advance the management of patients with MDR-TB the healthcare system (leadership of the hospitals and the caregivers for MDR-TB) should capture and utilize the views and experiences of the patients with MDR-TB and their families to pursue evidence informed decision making. The views and opinions of patients with MDR-TB, families of patients and the views of the caregivers for MDR-TB to identify treatment related issues and service needs and find the best solutions, options or strategies to address them.

6.2.4. MDR-TB infection control practices

6.2.4.1. Hospital level MDR-TB infection control practices

At the hospital level the activity of respiratory MDR-TB infection control was coordinated by the hospital MDR-TB panel team, which is composed of different categories of healthcare professionals. The study revealed that at treatment initiating centres (hospitals) there was optimum level of alertness and sound practice on respiratory MDR-TB infection prevention and control. Separation of infectious patients from culture converted ones, strict use of N95 and face masks and safe disposal of sputum cups are practiced at hospitals. However, as the premises of the hospital are not patient friendly, patients with MDR-TB usually inadvertently escape from the premise of the hospital MDR-TB treatment centre and mingle with the community. This was reported to be a potential risk for MDR-TB transmission to the community. The practice of escaping from the premises of the hospital by patients with MDR-TB is consistent with the report by Gandhi, Nunn, Dheda, Schaaf, Zignol, Soolingen, Jensen & Bayona 2010:1838) in which patients escaped from hospitals and even threaten or assault hospital staff and other patients in this regard.

6.2.4.2. Household level MDR-TB infection control practices

The result of this study noted that in the current programmatic management of MDR-TB there was no system for respiratory MDR-TB infection control at community, especially at the patients' household level. The proportion of MDR-TB cases infected by household contacts of an index patient with MDR-TB of this study was 8 (6%). Moreover, four of the eight cases diagnosed among contacts were diagnosed among household contacts of a single case in one family. This seems to be a warning sign regarding household level risk of respiratory MDR-TB infection in the study areas.

In a nutshell, the study revealed that the current practice of the programmatic management of MDR-TB in the study areas did not implement the minimum community (household) level respiratory MDR-TB infection control practice recommended by the national guideline on the programmatic management of MDR-TB in Ethiopia (Federal Ministry of Health 2014:150-51).

The result from the qualitative interviews with patients with MDR-TB and their caregivers revealed that, if family members attend to a patient with MDR-TB at the hospitals, the family members were given respirators (N95) as personal protective equipment. But once the patient is discharged from the hospital, the family member caregivers were not given respirators that they could use at household level. This means that, during patient admission to hospitals, patient attendants who are family members were given N95 if they attended to the patient with MDR-TB. But family members who were taking care of patients with MDR-TB at household level were not using respirators (N95) as a personal protective measure tool against MDR-TB infection.

The community and household level risk of infection to close contacts, revealed in this study, commensurate with the report by Caminero 2013:49-50, which indicated that household contacts to patients with MDR-TB are at an increased risk of infection with MDR-TB. The 6% proportion of MDR-TB infection among close contacts revealed in this study is higher than the 3% to 5.4% of MDR-TB diagnosed among close contacts reported in Peru (Becerra et al 2011:147).

As such, the absence of a functional system for respiratory MDR-TB infection prevention at community level, seemed to be a plausible risk factor for the observed high proportion of MDR-TB cases diagnosed among household contacts of index patients with MDR-TB.

There was no system or practice whereby caregivers from hospitals and treatment follow up centres visit patient's home to make arrangements regarding the living quarters of the patients with MDR-TB. Similarly, families of patients with MDR-TB were not oriented on the issue of respiratory MDR-TB infection. Furthermore, at household level, caretakers were not using respirators as personal protective tools. As a result, it is revealed in this study that significant numbers of patients with MDR-TB were diagnosed among household contacts of index patients with MDR-TB.

In summary, the increased actual risk of MDR-TB transmission to close contacts amplifies disease occurrence within families. The poor MDR-TB infection control and high prevalence of HIV among patients with MDR-TB, revealed in this study, allow an increase in the number of patients with MDR-TB in the community (Scardigli & Caminero 2013:208; Seddon et al 2012: 1343-44).

6.2.5. The model for enhancing the management of patients with MDR-TB

Development of a model for enhancing the management of patients with MDR-TB was one of the aims of the study. The objective of model development is to offer guidance in addressing the specific health problem in the programmatic management of MDR-TB (Fertman et al 2010:433). A healthcare model outlines the best practice for the delivery of care for the patient with a particular disease entity. A model facilitates implementation of the required change to improve the care and services that the patient receives (Pearson, Field & Jordan 2007:6).

The model for enhancing the management of patients with MDR-TB, has enabled understanding of the socio-demographic, socio-economic, clinical and programme policy context surrounding the care of the patient with MDR0-TB. Moreover, the model has identified the current state of practice in the care of patients with MDR-TB. The evidence generated was appraised, synthesed and used to inform all actors in the programme of MDR-TB through a model. According to Harvey & Kitson (2015:37,175), negotiations, spirits of collaboration and joint responsibility between clinicians caring for patients and the different departments who share the responsibility for the care and services needed by patients are important to overcome complex issues. For this, emphasis on shared

leadership that operates at multiple levels involving different people those works through strong communication is more effective than the role of individuals in leadership role. In this regard, the study revealed that, the communication among hospital managers, programme managers at provincial and town health offices and the caregivers for MDR-TB was weak. Moreover, the views and opinions of patients with MDR-TB and their families was not used to promote joint decision-making regarding the clinical care of patients with MDR-TB, and also in the planning and delivery of other services needed by patients with MDR-TB. To address these gaps the model has made recommendations that align with the national priority intervention to mitigate the problem of MDR-TB.

Thus, the model will assist evidence-informed practice by caregivers and programme managers at all levels. As such, the model will serve as a vehicle to drive the required change to mitigate the gaps in the management of patients with MDR-TB.

6.3. Summary

Chapter six presents the discussions on the results of the study in-line with the available literature. The next chapter, chapter 7, presents the conclusions and recommendations made based on the results of the current study.

Chapter 7: Conclusion and Recommendations

7.1. Introduction

This research endeavour employed a facility based cross-sectional, analytical, and a concurrent mixed methods design. Patients with MDR-TB from two different referral hospitals in the Oromia Region of Ethiopia were included in the study. The study has enabled to gain insight into the treatment outcomes of patients with MDR-TB and its determinants. The study has also enabled the researcher to understand the factors determining patients' perceived quality of care and level of patients' satisfaction with the care given for MDR-TB. To that end, a conceptual model was developed that was designed to enhance the management of patients with MDR-TB in the Oromia Region of Ethiopia and possibly in the other regions of the country. This chapter summarizes the key results of the study, conclusions, the limitations of the study and the recommendations made to improve the treatment outcomes of patients with MDR-TB. Recommendations were also made to improve patients' perceived quality of the care they received on MDR-TB and patients' satisfaction with the overall care and services offered for patients with MDR-TB.

7.2. Key results of the study

- There was high co-morbidity with MDR-TB among patients included in this study with 31% of the patients having had some co-morbidity with MDR-TB at the baseline and the majority of the co-morbidity was due to HIV/AIDS.
- A substantial number (64%) of the patients with MDR-TB had body mass index (BMI) of less than <18kg/m^2 at baseline, which was indicative of malnutrition.
- The composite treatment success rate for patients with MDR-TB included in this study was 69%,
- 27% of the patients with MDR-TB who were enrolled to the treatment for MDR-TB, died from the disease by the end of 24 month after commencing treatment.
- Compared to previous studies conducted in Ethiopia, there was a high death rate and a lower treatment success rate among patients with MDR-TB included in this study.
- Even though there was high MDR-TB and HIV/AIDS co-infection in the study area, the services needed for patients affected by both disease were not provided under one roof and

by the same caregiver. As such, patients affected by both diseases were obliged to seek care for HIV/AIDS in different facilities and with a different caregiver.

- Absence of standard laboratory based follow up services for patients on treatment for MDR-TB is evident
- The presence of any co-morbidity with MDR-TB at baseline including malnutrition was associated with an increased chance of death among patients with MDR-TB.
- Malnutrition among patients included in this study was further aggravated by the patients' weak social and economic status and the inadequate socio-economic support available for the patients by the programme of MDR-TB.
- The majority of patients treated for MDR-TB in the study areas were those who live under social and economic difficulties.
- The majority of patients with MDR-TB were employed in the informal sector with minimum daily wages
- MDR-TB results in loss of job and thereby loss of income. As such, MDR-TB aggravates already existing poor living conditions of the patients with MDR-TB and their families
- The current nutrition support given for patients with MDR-TB was not adequate both in terms of its quality and quantity. Some poor patients with MDR-TB who have dependents but do not have extra income, shared the nutrition items they were given with their family level dependents like the children
- The mode of delivery of the nutrition items was not patient centred. Patients were given a bucket of nutrition items at hospitals and they have to make an uncovered payment for transporting the nutrition items to their home areas.
- The financial support given for patients was inadequate to cover the direct and the indirect costs that patients with MDR-TB and their families incur due to the disease and in the course of their seeking care for it.
- The poor economic status of the patients and the inadequate level of nutrition support by the programme was a challenge for patients with MDR-TB to strictly adherence to a standard treatment schedule of MDR-TB. This impacts the patients' daily adherence to the lengthy treatment given for MDR-TB. As such, patients' social and economic difficulties had a potential impact on the treatment outcomes of patients with MDR-TB.

- For patients who live in remote rural areas and far away from the MDR-TB treatment follow up centres, no accommodation arrangements were made in the hometown of the treatment follow up centres. Such patients were exposed to an extra but unnoticed expense as they were obliged to pay for accommodation in the hometown of the treatment follow up centres until they completed the injection based intensive phase of the treatment given for MDR-TB.
- There was an encouraging level of communication between caregivers and patients at hospitals. The behaviour of the hospital level caregivers were described as empathic and caring. Yet, the status of communication between the caregivers and patients at the treatment follow up centres was revealed to be alienating.
- Patients' perceived quality of the care given for MDR-TB and patients' satisfaction with the overall care given for MDR-TB was suboptimal. Patients' satisfaction was affected by the inadequate socio-economic support, poor communication between patients and their caregivers and the low involvement of patients and their family caretakers in the patients' treatment decision making process.
- The absence of promptly responsive clinical care for patients' emergent medical care needs and the suboptimal service setups, including the cleanness of the patient's living rooms and toilets and the absence of recreational facilities in the compound of the hospital MDR-TB centres, has negatively affected the patients' perceived quality of care and their satisfaction with the care given for MDR-TB.
- There is a weak level of MDR-TB infection control practice at the community and the household level by the programme of MDR-TB.
    - Adequate health education was not given to patients with MDR-TB, families of the patients with MDR-TB and the community at large
    - Caregivers at the treatment follow up centres were not going to the patients' household level to provide health education for the family on MDR-TB. Moreover, inspection of the household level patients' living quarters was not done by caregivers to make arrangements for respiratory MDR-TB infection control at the household level before the patient was sent back to the community.
    - Patients with MDR-TB use the conventional public transport for whatsoever movement they make to seek care for MDR-TB including for the scheduled monthly follow up

services at the hospitals. The practice was found to be a potential risk factor for the transmission of MDR-TB to the community.

  - There was a high risk of MDR-TB transmission to household contacts of diagnosed index patients with MDR-TB. Family level caregivers of the patients with MDR-TB were not given personal protective equipments like the respirators.

- Community health extension workers were not involved in the current community based and ambulatory model of the treatment given for patients with MDR-TB.

7.3. Contribution of the study

In the Ethiopian context of the programmatic management of drug-resistant tuberculosis, this study assessed multiple factors that determine the treatment outcomes of patients with MDR-TB. It also assessed factors determining the process of the treatment given for MDR-TB, patients' adherence to treatment, patients' perceived quality of care and patients' satisfaction with the overall care given for MDR-TB.

As such, the result of this study has led to an understanding of the dynamics in the current programmatic management of MDR-TB in the Oromia Region of Ethiopia. The result of the study is expected to be useful in facilitating evidence informed decision making in the current national effort to scale up the programmatic management of MDR-TB in Ethiopia. The study has identified the dynamics in the healthcare delivery system and those at the level of healthcare facilities providing care for patients which determine the treatment outcomes of patients with MDR-TB, patients' perceived quality of care and patients' satisfaction with the care given for MDR-TB. The major contributions of this study are bulleted as follows:

- The study has identified the magnitude of the treatment outcomes of patients with MDR-TB who were enrolled to the treatment for MDR-TB
- Factors determining the treatment outcomes of patients with MDR-TB, patients' perceived quality of care and patients' satisfaction with care given for MDR-TB were identified.
- A conceptual model for enhancing the management of patients with MDR-TB (depicted in figure 5.1) was developed. The model depicts the relationship among the socio-

economic, programme policy, healthcare system, the patient and caregivers in determining the programmatic management of patients with MDR-TB.

- Based on the result of this study, the model will facilitate implementation of the various interventions to enhance the management of patients with MDR-TB.

7.4. Scope and limitations of the study

In an effort to get a maximally enriched understanding of the research problem, both quantitative and qualitative data were used to explain the different segments of the same research problem under investigation.

However, this study focused only on two referral hospitals found in the Oromia Region of Ethiopia, Adama Hospital Medical College and Nekemte Referral Hospital. These hospitals and the patients with MDR-TB who attended the same, might be different from patients with MDR-TB who attended hospitals in other regions of Ethiopia. The study used purposive sampling to identify and recruit participants. The qualitative component of the result was based on the reported experiences of the study participants. This is potentially subject to memory bias. It can also be subject to social desirability bias whereby participants might have told the researcher what they think is good to hear. Thus, the outcome of this study may be generalised with caution.

7.5. Recommendations

In view of the results of this study, the following were recommended for the scale up of the programmatic management of drug-resistant tuberculosis in the Oromia Region of Ethiopia:

7.5.1. Improve the socio-economic support for patients with MDR-TB

- Strengthen patient treatment enablers to improve patient adherence with the lengthy treatment given for MDR-TB. This should include the provision of adequate nutrition and financial support. The package of nutrition support given for patients, should consider family dependents of the patient with MDR-TB.
- By using locally available nutrition items, establish a scientifically appropriate and standard approach to the nutrition support provided for patients with MDR-TB.
- The system of delivery of the nutrition support should be patient centred. Hospitals should transport food items to the catchment treatment follow up centres so that the transportation cost incurred by patients to transport the food items to their household level decreases.
- Establish a system which will involve patients with MDR-TB and their family caretakers in shared decision making regarding the treatment and care of the patients and the nutrition and financial support that patients get from the programme of MDR-TB.
- The Health Bureau of the Oromia Region of Ethiopia needs to monitor and make sure that the food items included in the package of nutrition service provided to patients is adequate both in terms of quantity and quality to meet the nutrition requirements of patients with MDR-TB.
- The Health Bureau of the Oromia Region of Ethiopia needs to establish a strong monitoring mechanism to make sure that MDR-TB patients are getting the full package of the nutrition and financial support for which they are eligible.

7.5.2. Provide integrated service for MDR-TB and HIV co-management

- Build the capacity of caregivers for MDR-TB on the comprehensive clinical management of HIV/AIDS.
- Establish a system for the provision of drugs and supplies on HIV/AIDS to the MDR-TB centres and establish an anti-retroviral dispensing centre in the MDR-TB treatment centres.

- Provide services for both MDR-TB and HIV/AIDS under one roof and by the same caregivers at the MDR-TB treatment centres.
- Patients affected by both MDR-TB and HIV/AIDS, should be provided with clinical and laboratory follow up services by the same caregivers at the MDR-TB treatment centre.

7.5.3. Management of adverse drug reactions from second-line drugs

- Establish a dedicated laboratory unit for the MDR-TB treatment initiating centres of the hospitals so that second-line drug related adverse drug reactions could be diagnosed early.
- Strengthen the supply of ancillary drugs that are needed to treat the adverse drug-reactions from second-line drugs.
- Create compassionate and caring health caregivers at the MDR-TB treatment follow up centres.
- As the prevalence of adverse drug reactions is at its peak during the intensive phase of the treatment for MDR-TB, the provision of intensive service for the management of adverse drug reactions during the initial months of patient treatment for MDR-TB should be strengthened.

7.5.4. Emergency care for patients with MDR-TB

- Assign clinicians dedicated for the MDR-TB unit of the hospitals 7 days of a week and 24 hours of the day for patients with MDR-TB.
- Arrange a standby transport service to transport physicians when they are needed for emergency patient care.
- Continuously build the clinical skills of caregivers at the treatment follow up centres both through regular training and on-the-job clinical mentorship by caregivers at the hospitals.

7.5.5. Improve collaborative patient-caregiver communication

- Build the communication skills of the caregivers based at at the MDR-TB treatment follow up centres
- Improve the communication between caregivers and the patients with MDR-TB with a focus on caregivers practicing at the treatment follow up centres. Allocate 24 hour

emergency number for patients in order to improve communication between patients and caregivers.

- Improve the intensive involvement of psychiatric professionals with patients with clinical psychiatric problems
- The intensive involvement of the patients with MDR-TB in their treatment decision making process, will improve the perception of patients about caregivers and the perceptions of caregivers about patients with MDR-TB.
- Use the views and opinions of patients with MDR-TB and that of their families to identify gaps in the programmatic management of MDR-TB so that patient centred care and services can be provided.
- Build on the values and the experiences of patients with MDR-TB to strengthen programmatically effective and culturally appropriate communication practices.
- Provide empathic and caring clinical care along the continuum and help mitigating the multiple adverse effects of the treatment given for MDR-TB.

7.5.6. Improve the physical comfort of the premises of the MDR-TB treatment initiating centres at the hospitals

- Make the premises of the MDR-TB treatment initiating centre of the hospitals to be clean and recreative for patients treated at the MDR-TB treatment centres of the hospitals. Key interventions recommended include:
  - Assigning full-time cleaners to the hospital MDR-TB centre who can take care of the cleanness of the patients' living rooms (the beddings, floors), the toilets and the shower rooms.
  - Keep the compound and the hospital MDR-TB centre clean and create a homely environment to restrain patients from escaping from the treatment unit and highlight the importance of preventing transmission of the disease into the community.
- Establish functional recreative facilities in the compound of the MDR-TB centre that is dedicated for the patients with MDR-TB only:
  - Install functional television inside the patients' living rooms which helps prevent patients' being lonely and bored while staying in the MDR-TB centre. Alternatively,

there should be a comfortably designed TV room in the centre for patients as a group.

- Enable patients to have access to religious services by installing religious channels both for Christians and Muslims on the television. Through providing the hope of recovery for patients with MDR-TB, religious channels help to reduce the effect of drug related psychiatric problems among the patients.
- Provide easy to play games in the compound of the MDR-TB centre (bingo bowls, chess, or 'gebeta' (Ethiopian traditional game), etc).

7.5.7. Community based ambulatory treatment for patients with MDR-TB

- To help strengthen patients' coping ability to MDR-TB and its treatment, the programme of MDR-TB should strengthen community awareness on MDR-TB, with particular emphasis on the prevention of stigma against patients with the disease
- Engage the community health extension workers in the community based patient treatment support, MDR-TB infection prevention and tackling of stigma against patients with MDR-TB.
- Build the capacity of the health extension workers on the basics of the programmatic management of MDR-TB:
  - Train health extension workers on the basics of MDR-TB and on the skills of the daily observed treatment support provided for patients with MDR-TB in each county (kebele) from which a patient with MDR-TB is diagnosed.
  - The health extension workers shall take the lead responsibility in supervising the administration of the daily patient treatment under observation that is provided by the patients' family.
  - Through the health extension workers, make sure that patients can freely discuss their views and interests regarding the treatment they receive for MDR-TB. Provide and circulate brochures at schools and public spaces on MDR-TB. Local Radio stations in each area should broadcast programmes on MDR-TB. There should be a dedicated channel at the hospitals and treatment centres on MDR-TB issues, highlighting ways MDR-TB is transmitted, the need for adherence and why, the value

of nutrition while on treatment, the importance of cleanliness, when and how to take drugs for best results.

  - At the patients' home level, the health extension workers should provide ongoing counselling and treatment support and notify caregivers at the treatment follow up centres if and when a problem occurs

- Arrange accommodation services for patients with MDR-TB who live in rural areas and places far away from the treatment follow up centres who take a daily injection at the hometown of the treatment follow up centres.

7.5.8. MDR-TB infection control

- Raise the knowledge of patients, their household caregivers and the community on the danger of MDR-TB transmission among close contacts, especially household contacts
- Emphasise the high possibility of transmission through close contacts to the patients with MDR-TB. Caregivers at the treatment follow up centres and the health extension workers should implement the programmatically recommended MDR-TB infection control at the community and the household level.
- Before linking patients from the hospitals to the community based treatment and follow up services, arrangements should be made on respiratory MDR-TB infection control including the following:
  - Caregivers from the health centres should visit patients' living home space and inspects it, in collaboration with the patient's family, arrange a separate living room for the patient with MDR-TB.
  - Through community health education, raise the awareness of the general community on the basic concepts of MDR-TB, ways of its transmission and on the means of controlling its transmission
  - For families from whom a patient with MDR-TB is diagnosed, orient all members of the family on the basics of MDR-TB and its treatment and the role and responsibility of each family member in assisting the patient to complete the treatment given for MDR-TB
  - Orient the family on the dangers of the transmission of MDR-TB to the household contacts and other close contacts of the patient.

- Provide a respirator (N95) to household level caregivers of the patient with MDR-TB.

- Caregivers found at the treatment follow up centres should visit all patient's homes every quarter to track how the family is coping with the challenge of continuing to encourage the patient to adhere to the MDR-TB treatment, provide appropriate counselling, identify gaps and take timely action in collaboration with stakeholders in the healthcare system and the community.
- The health extension workers should provide regular health education for the family affected by MDR-TB and provide support on prevention of MDR-TB infection to household members of the diagnosed patients with MDR-TB
- Conduct active tracing of MDR-TB contacts and active MDR-TB case finding among household contacts of all diagnosed patients with MDR-TB.
- To mitigate the risk of possible MDR-TB infection at health facilities due to MDR-TB and HIV co-infected patients visiting different centres to seek care for MDR-TB and HIV/AIDS, provide services for both MDR-TB and HIV/AIDS under one roof.
- Caregivers from the treatment follow up centres should work towards enabling household contacts to visit health facilities for clinical evaluation quarterly and do so for a period of at least 2 years.
- Patients with MDR-TB use the conventional public transport during their monthly visit to the hospitals. The practice was found to be a potential risk factor for the transmission of MDR-TB to the community. Hospitals shall arrange, a monthly clinical follow up at the treatment follow up centres by a physician so that the risk of MDR-TB infection to the community is minimized.
- Ensure that a dedicated vehicle is available for the transportation of the patients, for linking patients back to the community level MDR-TB treatment and during the patients.
- Moreover, arrange a dedicated vehicle for transporting infectious patients from peripheral health facilities to hospitals.

7.6. Recommendations for future research

In the perspective of the results of this study, the following areas deserve further investigation:

1. Risk of respiratory MDR-TB infection among household contacts of index patients with MDR-TB and its determinants in Ethiopia.
2. Gender based differentials of MDR-TB treatment outcomes in Ethiopia.
3. Replicate the study in a different location, context, sample size and timeframe.

7.7. Conclusion

If the problem of MDR-TB and the factors determining the treatment outcomes of patients with MDR-TB are to be tackled successfully, the factors determining the treatment outcomes of patients with MDR-TB and factors determining patients' perceived quality of care and patients' satisfaction with the care given for MDR-TB need to be identified. In this regard, this study has identified socio-demographic and clinical factors that determine the treatment outcomes of patients with MDR0-TB. Moreover, the study has identified factors determining patients' perceived quality of care and patients' satisfaction with the care given for MDR-TB. Furthermore, the study has developed a conceptual model for enhancing the treatment of patients with MDR-TB in the study sites. Implementation of the model will effectively facilitate implementation of the required change to mitigate factors determining the treatment of patients with MDR-TB, patients' perceived quality of care and patient satisfaction with care given for MDR-TB.

In conclusion, it is with high confidence that the results from this study will enable health decision makers and caregivers for MDR-TB in the Oromia Region of Ethiopia to make evidence informed decisions regarding the MDR-TB programme design, programme management and resource allocation decisions during the subsequent national effort to expand the programmatic management of MDR-TB in Ethiopia.

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Annexes

Annexure 1: Results of the logistic regression model

Logistic Regression

Notes

Output Created		28-FEB-2017 12:09:42
Comments		
Input	Data	C:\Users\KeneaM\Desktop\Feb Analysis\ANALYSIS_FINAL DATA.sav
	Active Dataset	DataSet1
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	110
Missing Value Handling	Definition of Missing	User-defined missing values are treated as missing
Syntax		LOGISTIC REGRESSION VARIABLES OUTCOME /METHOD=FSTEP(LR) q3_SEX q7_8_BMI2 q16_AFB q21_RESTyp q25_COMORBID q57_HIV /CONTRAST (q3_SEX)=Indicator(1) /CONTRAST (q7_8_BMI2)=Indicator(1) /CONTRAST (q16_AFB)=Indicator(1) /CONTRAST (q21_RESTyp)=Indicator(1) /CONTRAST (q25_COMORBID)=Indicator(1) /CONTRAST (q57_HIV)=Indicator(1) /PRINT=GOODFIT CI(95) /CRITERIA=PIN(0.05) POUT(0.10) ITERATE(20) CUT(0.5).
Resources	Processor Time	00:00:00.03
	Elapsed Time	00:00:00.03

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	110	100.0
	Missing Cases	0	.0
	Total	110	100.0
Unselected Cases		0	.0
Total		110	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
Favourable treatment outcome	0
Unfavourable treatment outcome	1

Categorical Variables Codings

		Frequency	Parameter coding (1)
Patients HIV test result	0	83	.000
	Positive	27	1.000
BMI Categorized	0	44	.000
	=<18.5	66	1.000
Result of the diagnostic sputum smear examination	0	29	.000
	Smear Positive	81	1.000
What is the TB patient's resistance type	0	46	.000
	RR	64	1.000
Any co-morbid condition at baseline	0	76	.000
	Yes	34	1.000
Sex of the patient	Male	65	.000
	Female	45	1.000

Block 0: Beginning Block

Classification Table[a,b]

Observed			Predicted		
			Treatment category		Percentage Correct
			Favourable treatment outcome	Unfavourable treatment outcome	
Step 0	Treatment category	Favourable treatment outcome	76	0	100.0
		Unfavourable treatment outcome	34	0	.0
	Overall Percentage				69.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-.804	.206	15.199	1	.000	.447

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	q3_SEX(1)	4.564	1	.033
		q7_8_BMI2(1)	5.562	1	.018
		q16_AFB(1)	5.562	1	.018
		q21_RESTyp(1)	4.764	1	.029
		q25_COMORBID(1)	6.010	1	.014
		q57_HIV(1)	4.980	1	.026
	Overall Statistics		23.368	6	.001

Block 1: Method = Forward Stepwise (Likelihood Ratio)

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	5.819	1	.016
	Block	5.819	1	.016
	Model	5.819	1	.016
Step 2	Step	6.919	1	.009
	Block	12.737	2	.002
	Model	12.737	2	.002
Step 3	Step	5.431	1	.020
	Block	18.168	3	.000
	Model	18.168	3	.000
Step 4	Step	3.974	1	.046
	Block	22.142	4	.000
	Model	22.142	4	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	130.223[a]	.052	.073
2	123.304[a]	.109	.154
3	117.874[a]	.152	.215
4	113.899[b]	.182	.257

a. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001.

b. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	.000	0	.
2	1.266	2	.531
3	1.314	5	.933
4	4.198	7	.757

Contingency Table for Hosmer and Lemeshow Test

		Treatment category = Favourable treatment outcome		Treatment category = Unfavourable treatment outcome		Total
		Observed	Expected	Observed	Expected	
Step 1	1	58	58.000	18	18.000	76
	2	18	18.000	16	16.000	34
Step 2	1	44	45.042	10	8.958	54
	2	17	15.958	10	11.042	27
	3	14	12.958	8	9.042	22
	4	1	2.042	6	4.958	7
Step 3	1	21	21.000	2	2.000	23
	2	23	24.011	8	6.989	31
	3	5	4.621	1	1.379	6
	4	10	9.459	3	3.541	13
	5	9	8.368	7	7.632	16
	6	7	6.530	7	7.470	14
	7	1	2.011	6	4.989	7
Step 4	1	15	15.031	1	.969	16
	2	6	6.025	1	.975	7
	3	14	15.303	4	2.697	18
	4	10	9.545	2	2.455	12
	5	9	9.013	4	3.987	13
	6	9	6.435	1	3.565	10
	7	6	6.855	6	5.145	12
	8	3	3.709	6	5.291	9
	9	4	4.084	9	8.916	13

Classification Table[a]

Observed			Predicted		
			Treatment category		Percentage Correct
			Favourable treatment outcome	Unfavourable treatment outcome	
Step 1	Treatment category	Favourable treatment outcome	76	0	100.0
		Unfavourable treatment outcome	34	0	.0
	Overall Percentage				69.1
Step 2	Treatment category	Favourable treatment outcome	75	1	98.7
		Unfavourable treatment outcome	28	6	17.6
	Overall Percentage				73.6
Step 3	Treatment category	Favourable treatment outcome	68	8	89.5
		Unfavourable treatment outcome	21	13	38.2
	Overall Percentage				73.6
Step 4	Treatment category	Favourable treatment outcome	69	7	90.8
		Unfavourable treatment outcome	19	15	44.1
	Overall Percentage				76.4

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	q25_COMORBID(1)	1.052	.437	5.802	1	.016	2.864	1.217	6.743
	Constant	-1.170	.270	18.807	1	.000	.310		
Step 2[b]	q16_AFB(1)	-1.255	.483	6.765	1	.009	.285	.111	.734
	q25_COMORBID(1)	1.247	.465	7.184	1	.007	3.479	1.398	8.659
	Constant	-.360	.397	.822	1	.365	.698		
Step 3[c]	q7_8_BMI2(1)	1.117	.500	4.991	1	.025	3.056	1.147	8.142
	q16_AFB(1)	-1.142	.496	5.311	1	.021	.319	.121	.843
	q25_COMORBID(1)	1.369	.486	7.928	1	.005	3.930	1.516	10.191
	Constant	-1.209	.569	4.523	1	.033	.298		
Step 4[d]	q3_SEX(1)	.921	.467	3.883	1	.049	2.511	1.005	6.272
	q7_8_BMI2(1)	1.006	.508	3.922	1	.048	2.734	1.010	7.395
	q16_AFB(1)	-1.171	.502	5.446	1	.020	.310	.116	.829
	q25_COMORBID(1)	1.449	.498	8.484	1	.004	4.260	1.607	11.297
	Constant	-1.571	.609	6.657	1	.010	.208		

a. Variable(s) entered on step 1: q25_COMORBID.

b. Variable(s) entered on step 2: q16_AFB.

c. Variable(s) entered on step 3: q7_8_BMI2.

d. Variable(s) entered on step 4: q3_SEX.

Model if Term Removed

Variable		Model Log Likelihood	Change in -2 Log Likelihood	df	Sig. of the Change
Step 1	q25_COMORBID	-68.021	5.819	1	.016
Step 2	q16_AFB	-65.111	6.919	1	.009
	q25_COMORBID	-65.356	7.409	1	.006
	q7_8_BMI2	-61.652	5.431	1	.020
Step 3	q16_AFB	-61.635	5.397	1	.020
	q25_COMORBID	-63.103	8.333	1	.004
	q3_SEX	-58.937	3.974	1	.046
Step 4	q7_8_BMI2	-59.040	4.182	1	.041
	q16_AFB	-59.722	5.545	1	.019
	q25_COMORBID	-61.453	9.006	1	.003

Variables not in the Equation

			Score	df	Sig.
Step 1	Variables	q3_SEX(1)	5.258	1	.022
		q7_8_BMI2(1)	6.592	1	.010
		q16_AFB(1)	7.173	1	.007
		q21_RESTyp(1)	4.143	1	.042
		q57_HIV(1)	.062	1	.803
	Overall Statistics		18.432	5	.002
Step 2	Variables	q3_SEX(1)	5.224	1	.022
		q7_8_BMI2(1)	5.228	1	.022
		q21_RESTyp(1)	3.328	1	.068
		q57_HIV(1)	.020	1	.887
	Overall Statistics		11.887	4	.018
Step 3	Variables	q3_SEX(1)	3.991	1	.046
		q21_RESTyp(1)	2.630	1	.105
		q57_HIV(1)	.033	1	.855
	Overall Statistics		6.856	3	.077
Step 4	Variables	q21_RESTyp(1)	2.964	1	.085
		q57_HIV(1)	.088	1	.767
	Overall Statistics		3.026	2	.220

Annexure 2: Data collection tools

Part I: Structured questionnaire for the collection of the data on the clinical and programmatic management of patients with MDR-TB

General instruction: Data collector captures data available on MDR-TB patient chart; unit MDR-TB register; patient treatment card. When there is no data filled into any of the sources mentioned for any particular question, write 'no data'.

Date Questionnaire filled in: DD/MM/YY:_____Location/Facility:_____ _____
Questionnaire ID #:_____ Name of data collector:_____
Date the First Ever MDR-TB patient registered on facility Register? DD/MM/YY _____ Date the Last MDR-TB patient registered on facility Register: DD/MM/YY_____

Questions to assess programmatic management of drug-resistant tuberculosis at the two study sites **Source of data:** Unit MDR-TB register, individual MDR-TB patient chart & MDR-TB patient treatment card.
Questions Related to MDR-TB Patient's Socio-demographic Data
1. Patient Medical Registration Number (MRN):_____
2. Patient's unique MDR-TB Registration Number:_____
3. Sex of the Patient: 1. Male 2. Female
4. Age of the patient in completed years_____
5. Permanent residential address of the patient: Region_____ Zone/Province/_____; District/town_____
6. Patient's employment status. 1. Formally employed 2. Self-employed 3. Unemployed 4. Other (Specify)_____
7. Initial (pre-treatment) Weight (in Kgs):_____
8. Patient Height (in CMs)_____ BMI (kg/m^2):_____

9. Date patient escorted to the MDR-TB Treatment Initiating Centre:_____/ _____/_____ (Date/Month/Year)
10. Date patient initiated on second-line drugs:____/_____/_____(Date/Month/Year)
11. Does the TB patient have designated treatment supporter outside the TIC? 1. Yes 2. No 3. Unknown [if 'No' skip to 13]
12. If yes to question no. 11, who is the patient's treatment supporter? 1. Caregiver at TFC 2. Health Extension worker 3. Family member 4. Other (specify)_____
Current MDR-TB related Information of the Patient
13. What diagnostic method(s) was/were/ used to diagnose the patient with MDR-TB? [circle all that apply] **1**. Bacteriology (Smear microscopy) **2**. Bacteriology (culture) **3.** Genotypic (using GeneXpert) **4**. Genotypic (using Line Probe Assay) 5. Clinical (CXR & histopathology) 7**.** Other (specify)_____
14. Site of the TB Disease: 1. Pulmonary 2. Extra pulmonary 3. Both pulmonary & Extra pulmonary TB
15. What is the type of the TB case? **1**. Bacteriologically confirmed pulmonary TB **2.** Bacteriologically confirmed extra pulmonary TB **3.** Clinically diagnosed pulmonary TB 4**.** Clinically diagnosed extra pulmonary TB 5. Other (specify)_____
16. If TB is pulmonary and sputum smear examination was done, what is the result of the diagnostic sputum smear examination? 1. Smear Positive 2. Smear Negative 3. Unknown
17. If TB is pulmonary and diagnostic sputum was done, what was the semi-quantitative bacillary load reported at diagnosis? 1. **No AFB** (Negative)=0 AFB /100 HPF 2. **Scanty** (1+) =1-9 AFB/ 100 HPF 3. **Moderate** (2+) =10-99 AFB/100HPF 4. **High** (3+) = (1-10 AFB/1HPF/ 5. **Very High** (4+)/>10 AFB/1 HPF/
Use of Diagnostic Radiological Examination (Instruction: Data source is individual patient file/chart)
18. Was diagnostic radiological examination used for the patient? 1. Yes 2. No 3. Unknown [If 'No' or 'Unknown', skip to question 21]
19. If diagnostic radiography was used, what the extent of the baseline lung disease was as revealed by radiography: 1. Normal 2. Unilateral lesion 3. Bilateral lesion 4. Cavitation 5. Fibrosis 6. Other finding (specify)_____

20. If there was lung cavitary lesion at baseline, what is the extent of the cavitatary lesion? 1. Unilateral 2. Bilateral 3. Other type (specify) _____ **NB:** This data is collected from individual patient medical file/patient chart/.

21. What is the TB patient's resistance type: 1. RR 2. MDR-TB 3. Pre-XDR-TB 4. XDR-TB 5. Poly-resistant 6. Unknown

22. What is the MDR-TB patient's Registration group? 1. New 2. Relapse 3. Treatment after lost to follow ups 4. Treatment after failure of new regimen 5. Treatment after failure of re-treatment 6. Transfer in patient (T) 7. Other previously treated TB (O)

23. Does the patient have history of treatment with regimen containing any of the second-line anti-tuberculosis drugs? 1. Yes 2. No 3. Not known (If 'No' skip to Question 25)

24. If the patient has history of previous treatment with regimen containing second-line drugs, what was the patient's treatment outcome during treatment with regimen containing second-line drugs? 1. Cured 2. Treatment Completed 3. Treatment Failed 4. Lost to Follow Ups 5.Not evaluated (not known)

25. Is there any co-morbid condition at baseline? 1. Yes 2. No 3. Unknown (If 'No' skip to question 27)

26. If there is any co-morbidity at baseline, what was the co-morbid condition?: 1. Diabetes 2. Kidney Diseases 3. Hypertension 4. COPD 5.Liver Disease 6.HIV/AIDS 7. Psychiatric illness 8.HIV/AIDS related opportunistic infection (OIs) 9. Seizers 10. Other co-morbidities
(specify)_____

27. Is there any co-morbidity diagnosed in the course of patient treatment for MDR-TB? 1. Yes 2. No 3. Unknown (NB: This co-morbidity may be newly diagnosed for patients without co-morbidity at baseline & additional co-morbidity for patients with any co-morbidity at baseline)

28. If there is any co-morbidity diagnosed in the course of patient treatment, what was the co-morbidity? 1. Diabetes 2. Kidney diseases 3. Hypertension 4. Liver Disease 5. Psychiatric illness 6.Seizers 7.Other(specify)
_____

Questions related to practice of tracing household & close contacts of the index patient with MDR-TB

29. Number of household/close/ contacts living with the index patient. 1. None (alone) 2. 1-3 persons 3. 4-6 persons 4. 7-8 persons 5. 9-10 persons 6. Not Known (no evidence at TIC)

30. If the patient has contacts, are any of the contacts of the index MDR-TB patient traced? 1. Yes 2. No 3. Unknown (No evidence at the TIC) 4. Other practice (specify)_____(If 'No' or 'Unknown', skip to question 38 below)

31. If yes to question 30, how many household or close contacts of the index MDR-TB patient were traced? _____

32. If yes to question 30, how many of the traced household or close contacts were evaluated for TB clinically or through lab? _____

33. If yes to question 30, were there contacts screen positive for TB (presumptive TB)? 1. Yes 2. No [if 'no' skip to # 38]

34. Is DST done for contacts those found to be screen positive for TB? 1. Yes 2. No 3. Unknown

35. If DST was done for TB screen positive contacts, answer questions 35.1-35.5 (# of answers determined by # of DST available)

35.1. DST result for contact 1? **1**. No MTB **2**. MTB detected but no RR/MDR **3**. RR/MDR detected **4**. Indeterminate result

35.2. DST result for contact 2? **1**. No MTB **2**. MTB detected but no RR/MDR **3**. RR/MDR detected **4**. Indeterminate result

35.3. DST result for contact 3? **1**. No MTB **2**. MTB detected but no RR/MDR **3**. RR/MDR detected **4**. Indeterminate result

35.4. DST result for contact 4? **1**. No MTB **2**. MTB detected but no RR/MDR **3**. RR/MDR detected **4**. Indeterminate result

35.5. DST result for contact 5? **1**. No MTB **2**. MTB detected but no RR/MDR **3**. RR/MDR detected **4**. Indeterminate result

36. How many of the clinically or lab evaluated contacts of the index RR/MDR-TB patient were diagnosed with susceptible TB _____

37. How many of the clinically or lab evaluated contacts of index RR/MDR-TB were diagnosed with RR/MDR-TB? _____

38. If there is practice of tracing household and close contacts, what is the frequency of evaluation of contacts of known RR/MDR-TB patients? 1.Done only once 2.Quarterly 3.Every six month 4.Every year 5.Other schedule (specify) _____

39. For how long is a household/close/ contact of a confirmed RR/MDR-TB patient is followed? 1. For six months 2. For one year 3. For two years 4. For three years 5. For four years 6. Other practice or schedule (specify)_____

40. Result of drug-susceptibility testing (DST) for the patient: Enter all available DST results for the specified anti-tuberculosis drugs. [**Note:** R=Resistant; S= Susceptible; I= Indeterminate; U= DST result unknown or not done]

Drug	R	H	E	S	KM	Cm	Ofx	Am	Lfx	Mfx	Eto	Pto	Cs	PAS	Other	Other	Other
Resistance status	___	___	___	___	___	___	___	___	___	___	___	___	___	___	___	___	___

41. Date intensive phase MDR-TB treatment started (DD/MM/YY)_____
42. What is the MDR-TB regimen that the patient is taking (took) during intensive phase: (write regimen that is, drugs and duration)_____
43. What is the number of presumed effective second-line drugs used in the patient's MDR-TB treatment regimen during intensive phase (**NB**: do not count any first-line anti-tuberculosis drugs included in the regimen as one of presumed effective drug)?
    1. 2 drugs 2. 3 drugs **3**. 4 drugs **4.** 5 drugs **5**. Other (specify)_____
44. Total # of daily tablets given to the patient in the second-line regimen during intensive phase (include tablets of ancillary drugs, if any):_____
    _____
45. Date continuation phase MDR-TB treatment started (DD/MM/YY) _____[If patient died before entering continuation phase, skip to question 49]
46. What is the MDR-TB regimen that the patient is taking (took) during continuation phase: (write regimen that is drugs and duration)_____
    _____
47. What is the number of presumed effective second-line drugs used in the patients' MDR-TB treatment regimen during continuation phase? **1**. 2 drugs **2**. 3 drugs **3**. 4 drugs **4**. 5 drugs **5**. Other (Specify)_____
48. Total # of daily tablets given to the patient in the SLD regimen during continuation phase (include tablets of ancillary drugs, if any):
    _____
49. MDR-TB patient's Daily Observed Treatment (DOT) attendance:[**Instruction:** Note that the box is subdivided into upper and lower parts to fill in Daily Observed Treatment status for morning and evening does respectively in case a drug is given in divided doses. If daily dose of a given drug is given once, use upper box. Fill in: 3=if dose taken is Directly

Observed by treatment supporter; 2=if dose is taken by patient but not directly observed by treatment supporter and 1= if dose of the day not taken by the patient.

	DAYS IN A MONTH (ETHIOPIAN CALENDAR)																														
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
0																														
1																														
2																														
3																														
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50. Has the patient ever missed the daily dose of SLD? 1. Yes 2. No 3. Unknown (If 'No' or 'Unknown' skip to question 53).

51. If yes to question # 50, what is the number of daily dose of SLDs missed?
_____

52. If yes to question # 50, what was the reason for missing the doses? 1. Drug stock out 2. Patient failure to come for appointment 3. Drug-related adverse reactions 4. Other reason (specify)_____

53. Did the patient have history of treatment interruption (treatment discontinuation for less than 2 months) while on MDR-TB treatment? 1. Yes 2. No 3. Unknown

54. Did the patient have history of lost to follow ups (treatment discontinuation for two months or more) while on MDR-TB treatment? 1. Yes 2. No 3. Unknown

55. Is the patient tested for HIV? 1. Yes 2. No 3. Unknown (If 'No' skip to 63)

56. If tested for HIV, date HIV test done (DD/MM/YY)_____/_____/_____

57. If tested for HIV, HIV test Result of the patient. 1. Positive 2. Negative 3. Indeterminate (If answer is '2' skip to question # 63

58. If patient was positive for HIV, what was the baseline T-lymphocyte cell bearing (CD4) count (cells/mm3):_____

59. If patient was positive for HIV, was the patient given cotrimoxazole preventive therapy (CPT)? 1.Yes 2.No 3.Unknown (If 'No' skip to # 61)

60. If cotrimoxazole preventive therapy was given, Date the cotrimoxazole preventive therapy was started (DD/MM/YY)_____/_____/_____

61. If Positive for HIV was patient initiated on ART? 1. Yes 2. No 3. Unknown (If 'No' skip to # 63)

62. If ART was initiated, Date ART started (DD/MM/YY)_____/_____/_____

Questions related to assessing MDR-TB Patients' Bacteriological & Radiological follow up service status

63. **MDR-TB patient's Bacteriologic (sputum smear and culture) follow up status and its result:**

Instruction: Write 'N' for Culture (C) Negative result; 'P' for Culture (C) Positive Result; 'N' for sputum (S) negative result and 'P' for sputum (S) positive result and 'ND' if test not done or result not available both for culture and sputum for a scheduled month. **NB:** Date Specimen collected from a patient for a given follow up month is the same as date of follow up culture & sputum result of that month.

Type of Follow up	MONTH (0-24 month)																								
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Sputum (S)																									
Culture (C)																									

64. **Patient's Radiological Follow up status and its result (If 2 or 3 skip to 66):**

Availability of follow up radiological exam at each phase For each column fill: [1=If Done/available/ 2=If not done 3=Unknown (no data)]		
At Baseline	At End of Intensive Phase	At End of Treatment

65. Result of Follow up Radiological examination at each scheduled follow up time:

Result of Follow up Radiological exams at each phase: [Fill in: 1=Improved; 2=No change; 3=Deteriorated; 4=follow up result not available		
At Baseline	At End of Intensive Phase	At End of Treatment

66. If there was cavitary lesion at baseline (answer option '4'on Q19), what are the subsequent radiological changes in the lung cavitary lesion during scheduled radiological follow-ups? [Fill in: 1=Improved; 2=No change; 3=Deteriorated 4=follow up result not available (If there was no cavitary lesion at baseline skip to 67).

Level of Lung Cavities at each radiological examination		
At Baseline	At End of Intensive Phase	At End of Treatment

Questions to assess availability of continuum of care for patients with MDR-TB

67. If the patient was linked to catchment MDR-TB treatment follow up centres (TFCs), ask the following questions and if the patient is treated at TIC, that is 'No' to question # 11, skip to question # 68]

Note for data collector: The following activities are expected to be performed for an MDR-TB patient linked to TFCs. Data is obtained from individual patient file and from interview with TIC MDR-TB focal person (nurse):
67.1. Has contact tracing been completed for the patient? 1. Yes 2. No 3. Unknown (no evidence)
67.2. Has the discharge summary been completed for the patient? 1. Yes 2. No 3. Unknown (no evidence)
67.3. Are all SLDs related adverse event issues addressed for the patient linked to TFC? 1. Yes 2. No 3. Unknown (If treated at Tic, skip to 67.23).
67.4. Have housing arrangements been confirmed for the patient? 1. Yes 2. No 3. Not known (no evidence)
67.5. Have household level TB infection control arrangements been confirmed for the patient? 1. Yes 2. No 3. Unknown
67.6. How is the patient taken to TFC? 1. Escorted by TIC level caregivers; 2.Escorted by TFC level caregivers; 3.Escorted by immediate public health office; 4.Patient sent alone 5. Other means (specify) _____
67.7. Has a copy of the patient's treatment record been handed over to the patient or future care giver? 1. Yes 2. No 3. Unknown
67.8. On date of discharge has the date of the first follow-up appointment been arranged for the patient? 1. Yes 2. No 3. Unknown
67.9. Is the list of current medication (drugs) known to the patient? 1. Yes 2. No 3. Unknown (no evidence)

67.10. Is the list of current medication (drugs) known to the caregiver at TFC? 1. Yes 2. No 3. Unknown (no evidence)
67.11. For patients linked to TFCs, has access to medication been secured? 1. Yes 2. No 3. Unknown (no evidence)
67.12. Has the Daily Observed Treatment support been organized for the patient at TFC? 1. Yes 2. No 3. Unknown
67.13. Level where this patient gets Daily Observed Treatment support? 1. Health centre 2.Community/health post/ 3. Other (specify) _____
67.14. Is there confidence/evidence of certainty/ that the patient will continue taking the medication? 1. Yes 2. No 3. Unknown
67.15. Has a hospital contact number/person/ been handed over to the patient for advice? 1. Yes 2. No 3. Unknown
67.16. Has a hospital contact number/person/ been handed over to caregiver at the TFC for advice? 1. Yes 2. No 3. Unknown
67.17. Is the contact detail of the TB treatment supporter at TFC known to the hospital care giver? 1. Yes 2. No
67.18. Is the patient's contact address known to the hospital care giver? 1. Yes 2. No 3. Unknown
67.19. Is the patient's address known to the immediate public health office? 1. Yes 2. No 3. Unknown
67.20. Are treatment support services (e.g. nutrition & house rent, transport) available for the patient? 1. Yes 2. No 3. Unknown
67.21. Is the patient aware of the monitoring schedule during the outpatient phase of treatment? 1. Yes 2. No 3. Unknown
67.22. Is the care giver at TFC aware of the monitoring schedule during the outpatient phase of treatment? 1. Yes 2. No 3. Unknown
67.23. Do the hospital MDR-TB physician(s) have supportive contact with the national MDR/XDR-TB consilium (consulting group of professionals)? 1. Yes 2. No 3. Not known

67.24. If 'yes' to 67.23, what are the purpose of contact? 1. Management of difficult cases 2.Treatment of adverse drug reactions 3. Drugs and supplies related 4. Other (specify)_____

Questions to assess adverse events associated with treatment with second-line anti-tuberculosis drugs

68. Adverse drug associated with second-line drugs [**source of data**: MDR-TB Patient Treatment Card & Individual Patient Chart/file]

Instruction: '1' in the appropriate cell when the specified adverse drug reaction occurs & '2' when the adverse drug reaction does not occur at specified month	**Months of MDR-TB treatment**																								
Months of treatment	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
I. Gastro intestinal Disorders																									
Nausea & Vomiting																									
Abdominal pain																									
Diarrhea																									
Anorexia/appetite loss																									
Gastritis																									
Pubtic ulcer disease																									
II. Vestibular/ Ear / Disorders																									
Dizziness																									
Problem of imbalance																									
Hearing loss																									
III. Eye Related Disorders																									

Blurred vision																									
Photophobia																									
Decreased visual acuity																									
IV. Changes in clinical chemistry																									
Decreased K, Ca																									
Elevated ALT																									
Elevated creatinine																									
Elevated uric acid																									
hypomagnesemia																									
Hypothyroidism (TSH)																									
V. Musculo-skeletal disorders																									
Myalgia (muscle pain)																									
Arthralgia (joint pain)																									
Arthritis (inflammation involving the joint)																									
VI. Neurological Disorders																									
Dysgeusia (Metallic taste)																									
Peripheral neuropathy																									
Headache																									
Seizures																									
VII.Psychiatric Disorders																									
Anxiety																									

Insomnia																									
Psychosis																									
Depression																									
Suicidal attempts																									
VIII.Dermatological Disorders																									
Rash																									
Pruritus (itching)																									
Pain at site of injection																									
IX.Cardiovascular Related Disorder																									
Palpitation																									
Generalized weakness																									
Cor- pulmonale																									
Other cardiovascular disorders																									
X.Hypersensitivity reactions/immune related																									
Bronchospasm																									
Generalized urticarial/angioedema																									
Breathing difficulty																									
Anaphylaxis																									
Jaundice																									
Hemoptysis																									
Herpes zoster																									
XI.Other adverse drug reaction, if any (specify)																									
_____																									

69. For this patient has the MDR-TB treatment regimen ever been modified or permanently changed due to adverse drug reaction? 1. Yes 2.No 3. Unknown (If 'No' skip to question 71)
70. If the MDR-TB treatment regimen of the patient has ever been modified or permanently changed, what was/were/ the second-line anti-tuberculosis drug suspected?

    _____
71. Level of patient access to baseline and follow up clinical laboratory tests [**Instruction** for data collector: The patient weight in Kg is obtained from MDR-TB patient treatment card and the other lab results are attached to individual patient medical record/file so that patient file is source for all other lab test results except for weight; **NB**. At each month lab tests are done for ALT/SGPT, AST/SGOT, Creatinine, K, Ca, TSH, Hgb, WBC and pregnancy test. If test not done write "ND", if test is done write the actual lab result for that follow up month]

MONTH	Date	Weight (Kg)	ALT/SGPT	AST/SGOT	Creatinine	Uric Acid	K/Ca	Mg	TSH	Hgb	WBC	Pregnancy Test
Pre-treatment												
Month 0												
1												
2												
3												
4												
5												
6												
7												
8												
9												
10												
11												
12												
13												

14												
15												
16												
17												
18												
19												
20												
21												
22												
23												
24												

72. MDR-TB patient interim treatment outcome at 6 month of follow up? [asked for patients on treatment at least for 6-month] 1. Culture negative 2. Culture positive 3. Patient lost to follow ups 4. Died by 6-month 5. treatment outcome at 6 month not evaluated [If answer is '4' skip to 78]
73. What is current treatment status of the patient? 1. Currently on treatment 2. Treatment stopped/terminated 3. Other (specify)_____ [If answer is '1', skip to 78]
74. If treatment was stopped/terminated, date treatment stopped (DD/MM/YY)_____
75. Reason for termination of treatment: 1. Treatment successfully completed 2. Died 3. Lost to follow ups 4. Treatment Failed 5. Could not tolerate the regimen (ADRs) 6. Other reason (specify)_____
76. What is the patient's treatment outcome (ask for those that completed treatment or those for whom treatment outcome is assigned & circle the appropriate answer)? 1. Cured 2. Treatment Completed 3. Treatment Failed 4. Died 5. Lost to Follow Ups 6. Treatment outcome not evaluated
77. Date MDR-TB treatment outcome assigned for the patient (DD/MM/YY)_____

Post treatment follow up services for patients with MDR-TB (facility)

78. Is there practice of patient follow ups for patients released from treatment after completion of treatment? 1. Yes 2. No (If 'No' skip to question 81)
79. If yes to question 78, what is the **frequency** of **follow ups**? 1. Monthly 2. Quarterly 3. Bi-annually 4. Annually 5. Other (specify)____
80. If yes to question 78, **for how long** are patients followed after released from treatment? 1. Only once 2. For one year 3. For two years 4. Other (specify)_____
81. Are there cases of relapse among patients released from treatment after completion of treatment? 1. Yes 2. No 3. Unknown
82. Level of completeness and quality of data on each data source (that is Unit MDR-TB register, patient treatment cards, medical files, etc: **1**. Good **2**. Satisfactory **3**. Unsatisfactory **4**. Other observations (specify) _____

Part II: Checklist to assess status of hospital tb infection control implementation

[Instruction: General questions on MDR-TB infection control are filled through interview with hospital level focal person for MDR-TB]

1. Is there a functional l infection prevention (IP) committee in the hospital? 1. Yes 2. No
2. Is the MDR-TB focal person/nurse/ member of the hospital IP Committee? 1. Yes 2. No
3. Is TB infection risk assessment of the facility done and documented for the current fiscal year? 1. Yes 2. No
4. Does the facility have TB infection control plan for the current fiscal year? 1. Yes 2. No
5. Are the health care professionals providing care in the MDR-TB unit trained on TB IP? 1. Yes 2. No
6. Are the non-health care professionals providing care in the MDR-TB unit trained on TB IP? 1. Yes 2. No
7. Is the facility TB IC activity monitored (plan vs performance) and documented? 1. Yes 2. No

[Instruction: For the following questions, data is filled through observation of hospital's MDR-TB treatment unit & tape metre is used to measure distance between adjacent beds]

8. Is there room for isolation of inpatient MDR-TB patients? 1. Yes 2. No
9. If yes to question # 8, what type of MDR-TB patients are isolated? 1. Sputum positives 2. Culture positives 3. All pulmonary MDR-TB cases 4. All type of RR/MDR-TB patients are isolated from one another
10. If yes to question # 8, is one cohort of inpatient MDR-TB patients isolated from another cohort of MDR-TB patient? 1. Yes 2. No 3. Unknown
11. If no to question # 10, what is the major reason for not practicing isolation of MDR-TB patients of differing cohorts? 1. Absence of adequate room 2. Not usually enforced by the PMDT programme 3. Did not see the danger of infection 4. Other (specify)_____

12. Does the inpatient MDR-TB room have adequate cross ventilation (opposite windows/doors open all day)? 1. Yes 2. No
13. Do(es) the inpatient MDR-TB room(s) have access to natural light? 1. Yes 2. No
14. What is the distance between two adjacent beds of two MDR-TB patients? (measure distance from this patient's bed to all other adjacent beds & record average distance in metres):_____
15. Does each individual inpatient MDR-TB patient have sputum disposal container with proper lid 1. Yes 2. No 3. Unknown
16. Does every MDR-TB patient with pulmonary TB have a face mask? 1. Yes 2. No
17. Is there a shortage of supplies for MDR-TB infection control (N95 & facemasks)? **NB**: according to national guidelines one caregiver that is, nurse/doctor/paramedics needs 2 pieces of N95 per capita per week/? 1. Yes 2. No 3. 4. Unknown
18. What are practical challenges on TB IC in the facility?

_____

Part III: Semi-structured guide for in-depth interview with patients' with MDR-TB

I. Participants' socio-demographic background

Background information of the participants:
• Sex, age, marital status and residence, religion, occupation and level of education, • History of incarceration; Condition of use of substances (Alcohol, Khat and Cigarettes) • History of treatment for tuberculosis so far

II. Participant's level of awareness about MDR-TB and its risk factors

• What do you understand by the disease called MDR-TB?
• How do you think a person gets MDR-TB?
• Do you think that MDR-TB can be cured, explain?
• For how long do you think you are expected to take drugs given to treat your MDR-TB?
• Do you know the type of drugs you are expected to take for treatment of MDR-TB, describe? _____

III. Level of patient engagement in decisions making treatment initiation, follow up plans & issue of ADRs from SLDs.

- What discussions and agreements did you make with your caregivers at the inception of your treatment, please explain?
- Where place options are where you can take your treatment on MDR-TB (places where you can take your daily drugs) that you were told of at the beginning of your treatment?
- What do you think can be your role or responsibility while on treatment for MDR-TB?
- What type of health problems, if any, do you expect that you may encounter because of your taking drugs given for treatment of MDR-TB?

V. Participant's perceived socio-economic impact of becoming MDR-TB patient

- What costs do you think you or your families incur because of your catching MDR-TB and undergoing treatment for MDR-TB, explain?
- Do you think that your catching MDR-TB has deprived you of your regular income? If so describe in what ways?
- Do you think that your catching MDR-TB has deprived you of your regular social roles? If so, describe in what ways
- Who is responsible for taking care of other member of your family i.e. (if there are dependents)?
- During your stay at hospital (as inpatient), do you feel that you can be engaged in some livelihood activities i.e. able to work and earn some income, please explain!
- How do you describe your /your family's/ financial ability to cover expenses associated with seeking diagnosis and treatment services for MDR-TB?

V. Available treatment support schemes (treatment enablers) for MDR-TB Patients

- What is/are your means of making a living?
- Do you get nutrition support while on treatment for MDR-TB at this hospital, describe:
- If you get nutrition support, what are the packages in the food support that you get, describe!

- Do you get nutrition support when following treatment at follow up centres (health centres), please explain the situation including the packages in the food support you get.
- What challenges do you perceive with regards to nutrition support that you get (adequacy, patient centredness, etc.)?
- What things do you suggest that need to be improved regarding nutrition support done for MDR-TB patient like you?
- Do you get financial support to cover expenses related to seeking treatment for MDR-TB, please describe.
- What things do you suggest that need to be improved regarding financial support done for MDR-TB patient like you?

VI. Patients' level of satisfaction with Quality of clinical Care obtained on management of drug side effects!

- How do you describe your experience regarding overall quality of services you get from the hospital (TIC) & health centre (TFC) (explain by comparing what you actually get against what you expect from the hospital)
- How do you explain staff willingness to promptly help you on services you need both at TIC & TFC?
- How do you describe reliability of the staff and management of this hospital in providing promised services for MDR-TB patients, please explain.
- How do you describe your experience regarding availability of basic utilities (beds, toilets, utensils, etc) including place for recreation at the MDR-TB unit of this hospital?
- How do you interpret your experience regarding the sanitation of available basic utilities (beds, toilets, utensils, etc) including sanitation of the premises of the MDR-TB unit of this hospital?
- How do you interpret your experience regarding caregiver's willingness & commitment in providing the promised services (i.e. dependably/reliably/consistently/ and accurately)?
- In case you encounter health problems/complaints/pains/ while in hospital (TIC) or health centre (TFC), whom do you contact first?

- How do you explain your satisfaction with the quality of the medical treatment you receive from your caregivers for your complaints/pains? Explain.
- Do your caregivers listen to you carefully about your concerns and questions? Please explain.
- Are you treated with courtesy/politeness & respect by all staff that you encount here, describe:

VII. Condition of patients' accessibility to treatment initiating and treatment follow up centres

- How far is your permanent residence area from this hospital/town/? (KM)=_____
- How often do you come to this hospital to get the services you need, describe? _____
- Do you face challenges in attending appointments with this hospital, please mention! _____
- How often do you go to the Health Centre where you follow your treatment, what problems do you face?
- What good things did you experience during your treatment for MDR-TB? What challenges/bad things did you experience?
- What things do you recommend be improved for MDR-TB patients like you to enable them to comfortably follow their treatment?
- Is there anything, if any that you want to add or recommend that you feel need improvement to assist MDR-TB patients like you?

Part IV: Semi-structured interview guide for in-depth interview with caregivers for MDR-TB

I. Caregiver's Professional background:

- Professional background
- Department of assignment in his/her facility
- Types of in-service trainings taken by the participant
- Experience in years

II. Caregiver's practice in providing the daily directly observable treatment (DOT)support for MDR-TB patients on second-line drugs (SLDs)

1. What is the number of directly observable treatment days' per week for the oral second-line drugs? How many are the daily directly observable treatment days for

	oral second-line drugs do you have per week? _____
2.	What is the number of directly observable treatment days' per week for the injectable second-line drugs? How many are the directly observable treatment days for injectable second-line drugs do you have per week? _____
3.	What scheme is available (responsible body) to make sure that patients are treated under strict Daily Observed Treatment support at: 1. Treatment initiating centre (hospital)? _____ 2.Treatment follow up centre (health centres)? _____
4.	What treatment enablers, if any, are available for MDR-TB patients? _____
5.	If there is a scheme to provide enablers for patients, does the facility have written records/evidence on treatment enablers given to the patient, describe (like data on disbursement of food or finance)._____
6.	What is your view on the need for an incentive scheme for caregivers for MDR-TB? _____
7.	If you recommend an incentive schemes for MDR-TB caregivers, what do you think should be the form of the incentive?_____
III.	**Management of second-line drug (SLDs) related adverse drug reactions**
8.	What are the most frequently encountered challenges in the clinical management of MDR-TB patients? _____
9.	What factors determine the management of adverse events from SLDs immediately & appropriately? _____
IV.	**Hospital practice on MDR-TB patient Follow ups:**
10.	How do you communicate with your MDR-TB patients after they are linked to satellite health centres to continue treatment? _____
11.	If there is a prescheduled date for contact between caregivers & patients followed at the health centres, what are the major support activities given during contact (clinical and non-clinical)? _____
12.	What supportive system is available to deal with challenges faced during the lengthy patient treatment (like tracing patients lost to follow ups/is the hospital management and immediate health authority supportive? _____

13. What forums are available for contact between caregivers at this hospital and those found at the catchment MDR-TB treatment follow up centres?_____
14. How do you describe functionality status of referral linkage between your hospital & catchment TFCs? _____
15. Are there schemes in place for follow ups of MDR-TB patients that have completed treatment? 1. Yes 2. No. If yes, what is the frequency and duration of follow ups after treatment is completed? _____
16. How do you describe the current status of MDR-TB patients in taking responsibility for their own treatment? What do you recommend be done in the future? _____
V. TB Laboratory Specimen Referral, Transportation and feedback related questions
17. Is there a system for referral of samples of MDR-TB patients? (diagnostic & referral) 1. Yes 2. No 3. Does not know
18. Please describe your level of satisfaction with available sample referral system_____
19. Are laboratory results available when needed?describe_____
20. Is there interaction between central lab staff and clinicians at your hospital? 1. Yes 2. No
21. If yes, go to question 24, what is the main mode of this interaction? Pplease describe _____
22. What is the average number of samples of MDR-TB cases for whom culture sample are sent to a referral lab per month?
23. What is the average number of culture specimens on which feedback result are obtained per month?
24. What are the challenges you face in the current specimen referral system? _____
25. What improvements would you like to see in the specimen referral system? _____
26. What are the things you feel need improvement in the implementation of PMDT in this hospital/country? [explain briefly]_____

VI.	**Health System support to the PMDT at the hospital**
27.	Do you feel supported by the hospital management on PMDT? (please describe)_____
28.	Do you feel supported by the immediate health office on PMDT? (please describe)_____
29.	Is the MDR-TB programme perceived as a district/zone/town health problem and not as MDR-TB treatment centre problem? (please describe)
30.	Are staff members at PHCU adequately trained to manage MDR-TB patients referred to TFCs? _____
VII.	**Level of integration of services on MDR-TB and comprehensive HIV/AIDS services**
31.	Have you ever had MDR-TB patients who are co-infected with HIV? _____
32.	Are the caregivers for MDR-TB found at this facility trained on comprehensive HIV/AIDS including ART? _____
33.	Are the MDR-TB and HIV services integrated (ART service available in the MDR-TB unit for the co-infected)? Describe:_____
34.	If the MDR-TB and HIV services are not integrated, where do the MDR-TB-HIV co-infected patients get services on HIV/AIDS? _____
35.	Is the PMDT data/clinical practice & expertise of this hospital used by central consulium for national PMDT decision making or management of M(X)DR-TB patients (describe)_____

Annexure 3: Ethical clearance certificates

Annexure 3.1. Ethical clearance certificate from the the University of South Africa-Department of Health Studies Higher Degrees Committee

UNISA university of south africa

UNIVERSITY OF SOUTH AFRICA
Health Studies Higher Degrees Committee
College of Human Sciences
ETHICAL CLEARANCE CERTIFICATE

REC-012714-039

HSHDC/442/2015

Date: 25 November 2015 Student No: 5766-162-6

Project Title: Assessment of treatment outcome and associated factors among MDR-TB patients enrolled to second line anti-TB drugs in Ethiopia.

Researcher: Mengistu Kenea Wakjira

Degree: D Litt et Phil Code: DPCHS04

Supervisor: Prof PT Sandy
Qualification: PhD
Joint Supervisor: -

DECISION OF COMMITTEE

Approved [√] **Conditionally Approved** [ ]

Prof L Roets
CHAIRPERSON: HEALTH STUDIES HIGHER DEGREES COMMITTEE

Prof MM Moleki
ACADEMIC CHAIRPERSON: DEPARTMENT OF HEALTH STUDIES

PLEASE QUOTE THE PROJECT NUMBER IN ALL ENQUIRES

Annexure 3.2. Ethical clearance certificate from the University of South Africa-Ethiopia Centre for Graduate Studies

UNISA university of south africa

16 AUGUST, 2016

UNISA-ET/KA/ST/29/16-08-16

OROMIA REGION HEALTH BUREAU

ADDIS ABABA

Dear Madam/Sir,

This is to confirm that Mr. Mengistu Kenea Wakjira (student number 57661626) is a PhD student in the Department of Health Studies at the University of South Africa (UNISA). Currently, he is at the stage of data collection on his Doctoral research entitled ***"Assessment of treatment outcome and its determinants among MDR-TB patients enrolled to second-line anti-TB drugs at Referral Hospitals in Ethiopia."***

This is therefore to kindly ask you to please assist the student to get ethical clearance from your Bureau that enables him to collect the necessary data. Attached, please find the copy of the Ethical Clearance he secured from the Department of Health Studies, UNISA.

Sincerely,

for

Tsige GebreMeskel Aberra

UNISA REGIONAL LEARNING CENTRE
PO BOX 13635 ADDIS ABABA ETHIOPIA
TEL +251-114-350141
+251-114-350078
FAX +251-114-351245
MOBILE +251-912-191483

Deputy Director – Academic and ICT Support

UNISA – ETHIOPIA Centre of Graduate Studies

Annexure 3.3. Ethical clearance certificate from the Oromia Region Health Bureau, Public Health Emergency management and Health Research core-process to the Adama Hosptal Medical College

BIIROO EEGUMSA FAYYAA OROMIYAA

OROMIA HEALTH BUREAU

Lakk/Ref. No BEPD/AHOPDD/1-8/2291

Guyyaa/Date 20-12-2008

To ***Adama Hospital Medical College***

Adama

Subject: Support for Mr. Mengistu Kenea Wakjira to get access to data for his studies at UNISA

Dear Madam/Sr:

In its letter written to our regional health bureau datec 16 August, 2016; ref. No.UNISA-ET/KA/ST/29/16-08-16, University of South Africa-Ethiopia Center for Graduate Studies has confirmed us that Mr. Mengistu Kenea Wakjira (student number 57661626), is a PhD student at the University of South Africa and that currently he is planning to collect data for his Doctoral research entitled "Assessment of treatment outcome and its determinants among MDR-TB patients enrolled to second-line anti-TB drugs at referral hospitals in Ethiopia". In this way the University of South Africa has requested our bureau to assist the student to get ethical clearance from our bureau to enable him get the necessary data.

Thus we hereby notify your hospital to assist Mr. Mengistu Kenea Wakjira in getting access to data he needs from your hospital for his research. Here attached with this letter please find the ethical clearance he secured from University of South Africa and from UNISA-Ethiopia Center for graduate studies.

Regards,

Gemechu Shume
Public Health Emergency Management & Health Research Core Process Manager (BSC,MPH)

Tessoo: Tel: 011-371-72-27,011-371-72-77 P.O. Box. 24341 E-mail: ohbhead@telecom.net.et
Address: ADDIS ABABA/FINFINNE-ETHIOPIA

Annexure 3.4: Ethical clearance certificate from the Oromia Region Health Bureau, Public Health Emergency management and Health Research core-process to the Nekemte Referral Hospital

BIIROO EEGUMSA FAYYAA OROMIYAA

OROMIA HEALTH BUREAU

Lakk/Ref. No. [illegible]/2794

Guyyaa/Date 24-12-2008

To **Nekemte Referral Hospital**

Nekemete

Subject: Support for Mr. Mengistu Kenea Wakjira to get access to data for his studies at UNISA

Dear Madam/Sr:

In its letter written to our regional health bureau dated 16 August, 2016; ref. No.UNISA-ET/KA/ST/29/16-08-16, University of South Africa-Ethiopia Center for Graduate Studies has confirmed us that Mr. Mengistu Kenea Wakjira (student number 57661626), is a PhD student at the University of South Africa and that currently he is planning to collect data for his Doctoral research entitled "Assessment of treatment outcome and its determinants among MDR-TB patients enrolled to second-line anti-TB drugs at referral hospitals in Ethiopia". In this way the University of South Africa has requested our bureau to assist the student to get ethical clearance from our bureau to enable him get the necessary data.

Thus we hereby notify your hospital to assist Mr. Mengistu Kenea Wakjira in getting access to data he needs from your hospital for his research. Here attached with this letter please find the ethical clearance he secured from University of South Africa and from UNISA-Ethiopia Center for graduate studies.

Regards,

Gemechu Shume
Public Health Emergency Management & Health Research Core Process Manager (BSC,MPH)

Tessoo: Tel: 011-371-72-27,011-371-72-77 P.O. Box. 24341 E-mail: ohbhead@telecom.net.et
Address: ADDIS ABABA/FINFINNE-ETHIOPIA

Annexure 4: Information sheet & informed consent for participants of the in-depth interviews with patients with MDR-TB and their caregivers

Good morning/afternoon…My name is "Mengistu Kenea Wakjira" and I am a PhD student at UNISA. Currently I am collecting data for my thesis entitled *Factors determining treatment outcomes among MDR-TB patients enrolled to second-line anti-tuberculosis drugs at Adama Hospital Medical College and Nekemte Referral hospital.*

I would also like to explore MDR-TB patients' perceptions on the quality of care and services they receive at this hospital and their satisfaction. The main objective of this research is to contribute to improving quality of care and clinical services provided for MDR-TB patients in hospitals like this. Thus, the research will come up with findings and recommendations that guide resource allocation and decision making regarding programmatic management of drug-resistant TB so that the services could possibly be improved.

In this way, I would like to know your views on quality of MDR-TB care that you are given at this hospital *(patients); y*our practices & perceptions on the programmatic management of drug-resistant TB at this hospital *(caregivers).* Your participation will be appreciated. The results of this study will help to better understand factors determining satisfaction of patients like you towards the care given and factors determining MDR-TB treatment outcomes. Your participation in this research is entirely voluntary and if you feel uncomfortable and decide to withdraw at any time, you are free to withhold participation. Your decision not to participate will not have any impact on the care and services you get at this hospital.

Moreover, if you deciding to continue participating in the study and you feel uncomfortable to respond to some of the questions or to discuss some issues, you can skip such questions and discussions without any precondition. The interview will last about 30 minutes. The interview will be strictly confidential and the responses will not be shared with anyone. We would like to ask for your permission to tape record the interview in order to record your responses accurately and not miss any of your valued input. Your interview responses will be combined with responses from other respondents and no one will be able to identify your individual responses and link them back to participants. The information gathered will only be used for the stated purpose. We will not mention your name or address anywhere outside this room. I will be using a number code instead of names which will further conceal your identity and guarantee confidentiality.

In case you need assistance on issues related to MDR TB and its treatment or want to discuss personal issues at any time while on treatment for MDR-TB or beyond this discussion, you may contact me: Mengistu Kenea Wakjira; Address: Addis Ababa, Cell phone:+251-911-30-25-68; Email:-mkenea@yahoo.com; mengistukenea@gmail.com or 57661626@mylife.unisa.ac.za

By signing below, you confirm that this form has been explained to you and that you understand its contents.

1. AGREE TO PARTICIPATE 2. I DO NOT AGREE TO PARTICIPATE

Instruction for data collector: If the answer is 2 (above), thank the patient and allow him/her to depart. If the answer is 1 (above), first ask the participant to sign on the line below and continue the interview:

Interviewee's signature _____ Date_____